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=> d his ful

     (FILE 'HOME' ENTERED AT 16:12:32 ON 03 AUG 2006)

     FILE 'HCAPLUS' ENTERED AT 16:12:46 ON 03 AUG 2006
                E VALE RONALD D/AU
L1           145 SEA ABB=ON  ("VALE RON D"/AU OR "VALE RONALD"/AU OR "VALE
                RONALD D"/AU OR "VALE RONALD DAVID"/AU)
                E HARTMAN JAMES J/AU
L2             9 SEA ABB=ON  ("HARTMAN JAMES J"/AU OR "HARTMAN JAMES JOSEPH"/AU)
L3             3 SEA ABB=ON  L1 AND L2
L4               ANALYZE L3 2 CT :      27 TERMS

     FILE 'REGISTRY' ENTERED AT 16:30:58 ON 03 AUG 2006
                E TUBULIN/CN
L5          1239 SEA ABB=ON  TUBULIN?/CN
                E DAPI/CN
L6             1 SEA ABB=ON  DAPI/CN
                E ANS/CN
L7             2 SEA ABB=ON  ANS/CN
L8             1 SEA ABB=ON  82-76-8
                E BIS-ANS/CN
L9             2 SEA ABB=ON  BIS-ANS/CN
                E NPN/CN
L10            1 SEA ABB=ON  "NPN 3"/CN
                E N-PHENYL-1-NAPHTHYLENE/CN
                E NAPHTHYLENE/CN
L11            1 SEA ABB=ON  "NAPHTHYLENE DIISOCYANATE"/CN
                E RUTHENIUM RED/CN
L12            2 SEA ABB=ON  "RUTHENIUM RED"/CN
                E CRESOL VIOLET/CN
                E DCVJ/CN
L13            1 SEA ABB=ON  DCVJ/CN
                E CRESOL/CN
L14            1 SEA ABB=ON  "CRESOL FAST VIOLET"/CN
L15           11 SEA ABB=ON  L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13
                OR L14
L16         1250 SEA ABB=ON  L15 OR L5
L17            0 SEA ABB=ON  L16 AND (?FLUOROMETRY? OR ?FLUORESENC?)

     FILE 'HCAPLUS' ENTERED AT 16:41:47 ON 03 AUG 2006
L18         4645 SEA ABB=ON  L16
L19          287 SEA ABB=ON  L18 AND (?FLUOROMETRY? OR ?FLUORESENC?)
L20           11 SEA ABB=ON  L19 AND DRUG(W)SCREEN?
L21            7 SEA ABB=ON  L19 AND (?MONOMER? OR ?DIMER? OR ?OLIGOMER?)
L22            1 SEA ABB=ON  L19 AND ?MICROTUBUL?(4A)?SEVER?
L23            1 SEA ABB=ON  L19 AND ?TUBUL?(4A)?SEVER?
L24           17 SEA ABB=ON  L20 OR L21 OR L22
L25           15 SEA ABB=ON  L24 AND (PRD<20040120 OR PD<20040120)

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, WPIDS' ENTERED AT
     16:46:33 ON 03 AUG 2006
L26            9 SEA ABB=ON  L24
L27            9 DUP REMOV L26 (0 DUPLICATES REMOVED)

     FILE 'USPATFULL' ENTERED AT 16:48:14 ON 03 AUG 2006
L28           22 SEA ABB=ON  L24 AND (PRD<20040120 OR PD<20040120)

     FILE 'HCAPLUS' ENTERED AT 17:05:32 ON 03 AUG 2006
L29        31490 SEA ABB=ON  L16 OR ?TUBULIN? OR ?DAPI? OR ?ANILINONAPHTHALENE?(
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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              W)?SULFONATE? OR ANS OR BIS(W)ANS OR BIS(W)?ANILINONAPHTHALENE?
              (W)?SULFONATE? OR N(W)PHENYL(W)1(W)?NAPHTHYLENE? OR NPN OR
              ?RUTHENIUM?(W)RED? OR ?CRESOL?(W)?VIOLET? OR DCVJ OR ?JULOLIDIN
              E?
L30         479 SEA ABB=ON  L29 AND (?FLUOROMETRY? OR ?FLUORESENC?)
L31          18 SEA ABB=ON  L30 AND  DRUG(W)(SCREEN OR SCREENING)
L32          25 SEA ABB=ON  L30 AND (?MONOMER? OR ?DIMER? OR ?OLIGOMER? OR
                ?MICROTUBUL?(5A)?SEVER? OR ?TUBUL?(4A)?SEVER?)
L33          40 SEA ABB=ON  L31 OR L32
L34           8 SEA ABB=ON  L33 AND ?TEST?
L35          40 SEA ABB=ON  L34 OR L33

    FILE 'REGISTRY' ENTERED AT 17:13:49 ON 03 AUG 2006
L36           2 SEA ABB=ON  (AVIDIN OR BIOTIN)/CN

    FILE 'HCAPLUS' ENTERED AT 17:14:13 ON 03 AUG 2006
L37           4 SEA ABB=ON  L35 AND (?MICROTUBUL?(W)?MOTOR?(W)?PROTEIN? OR L36
                OR ?AVIDIN? OR ?BIOTIN? OR ?ANTI?(W)?TUBULIN(W)?ANTIBOD? OR
                ?MICROTUBUL?(W)?BIND?(W)?PROTEIN? OR MAP)

    FILE 'REGISTRY' ENTERED AT 17:15:55 ON 03 AUG 2006
L38           6 SEA ABB=ON  (POLYARGININE OR POLYHISTIDINE OR POLYLYSINE)/CN

    FILE 'HCAPLUS' ENTERED AT 17:17:12 ON 03 AUG 2006
L39           1 SEA ABB=ON  L35 AND (?POLYARGININE? OR ?POLYHISTIDINE? OR
                ?POLYLYSINE?)
L40           1 SEA ABB=ON  L35 AND ?CONTACT?(4A)(?TUBULIN? OR ?MICROTUBULE?)
L41          40 SEA ABB=ON  L35 OR L37 OR L39 OR L40
L42          35 SEA ABB=ON  L41 AND (PRD<20040120 OR PD<20040120)
L43           1 SEA ABB=ON  L42 AND ?DEPOLYMERIZ?(4A)?INHIBIT?
L44          35 SEA ABB=ON  L42 OR L43 35 cits from CAPlus

    FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 17:19:14 ON
    03 AUG 2006
L45          34 SEA ABB=ON  L41
L46          33 DUP REMOV L45 (1 DUPLICATE REMOVED) 33 cits from

    FILE 'USPATFULL' ENTERED AT 17:28:04 ON 03 AUG 2006

    FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 17:28:21 ON
    03 AUG 2006
L47           0 SEA ABB=ON  L46 AND ?DEPOLYMERIZ?(4A) ?INHIBIT?

    FILE 'USPATFULL' ENTERED AT 17:28:49 ON 03 AUG 2006
L48         280 SEA ABB=ON  L42 OR L43
L49           2 SEA ABB=ON  L48 AND ?DEPOLYMERIZ?(4A)?INHIBIT? 2 cits from
                                                               USPatFull
    FILE HOME

    FILE HCAPLUS

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FILE COVERS 1907 - 3 Aug 2006 VOL 145 ISS 6
FILE LAST UPDATED: 1 Aug 2006 (20060801/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 AUG 2006 HIGHEST RN 897851-29-5
DICTIONARY FILE UPDATES: 1 AUG 2006 HIGHEST RN 897851-29-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE MEDLINE
FILE LAST UPDATED: 2 Aug 2006 (20060802/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 2 August 2006 (20060802/ED)

FILE EMBASE
FILE COVERS 1974 TO 3 Aug 2006 (20060803/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 3 APR 2006 <20060403/UP>
FILE COVERS APRIL 1973 TO DECEMBER 22, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE. USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHER DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION ABOUT THE IPC REFORM <<<

FILE JICST-EPLUS
FILE COVERS 1985 TO 24 JUL 2006 (20060724/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE WPIDS
FILE LAST UPDATED: 1 AUG 2006 <20060801/UP>
MOST RECENT DERWENT UPDATE: 200649 <200649/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 3 Aug 2006 (20060803/PD)
FILE LAST UPDATED: 3 Aug 2006 (20060803/ED)
HIGHEST GRANTED PATENT NUMBER: US7086090
HIGHEST APPLICATION PUBLICATION NUMBER: US2006174388
CA INDEXING IS CURRENT THROUGH 1 Aug 2006 (20060801/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 3 Aug 2006 (20060803/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2006

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=> log hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    9.43      887.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY     SESSION
CA SUBSCRIBER PRICE                                    0.00      -39.75

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:33:46 ON 03 AUG 2006
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=> d que stat l44
L5        1239 SEA FILE=REGISTRY ABB=ON  TUBULIN?/CN
L6           1 SEA FILE=REGISTRY ABB=ON  DAPI/CN
L7           2 SEA FILE=REGISTRY ABB=ON  ANS/CN
L8           1 SEA FILE=REGISTRY ABB=ON  82-76-8
L9           2 SEA FILE=REGISTRY ABB=ON  BIS-ANS/CN
L10          1 SEA FILE=REGISTRY ABB=ON  "NPN 3"/CN
L11          1 SEA FILE=REGISTRY ABB=ON  "NAPHTHYLENE DIISOCYANATE"/CN
L12          2 SEA FILE=REGISTRY ABB=ON  "RUTHENIUM RED"/CN
L13          1 SEA FILE=REGISTRY ABB=ON  DCVJ/CN
L14          1 SEA FILE=REGISTRY ABB=ON  "CRESOL FAST VIOLET"/CN
L15         11 SEA FILE=REGISTRY ABB=ON  L6 OR L7 OR L8 OR L9 OR L10 OR L11
               OR L12 OR L13 OR L14
L16       1250 SEA FILE=REGISTRY ABB=ON  L15 OR L5
L29      31490 SEA FILE=HCAPLUS ABB=ON  L16 OR ?TUBULIN? OR ?DAPI? OR
               ?ANILINONAPHTHALENE?(W)?SULFONATE? OR ANS OR BIS(W)ANS OR
               BIS(W)?ANILINONAPHTHALENE?(W)?SULFONATE? OR N(W)PHENYL(W)1(W)?N
               APHTHYLENE? OR NPN OR ?RUTHENIUM?(W)RED? OR ?CRESOL?(W)?VIOLET?
                OR DCVJ OR ?JULOLIDINE?
L30        479 SEA FILE=HCAPLUS ABB=ON  L29 AND (?FLUOROMETRY? OR ?FLUORESENC?
               )
L31         18 SEA FILE=HCAPLUS ABB=ON  L30 AND  DRUG(W)(SCREEN OR SCREENING)
L32         25 SEA FILE=HCAPLUS ABB=ON  L30 AND (?MONOMER? OR ?DIMER? OR
               ?OLIGOMER? OR ?MICROTUBUL?(5A)?SEVER? OR ?TUBUL?(4A)?SEVER?)
L33         40 SEA FILE=HCAPLUS ABB=ON  L31 OR L32
L34          8 SEA FILE=HCAPLUS ABB=ON  L33 AND ?TEST?
L35         40 SEA FILE=HCAPLUS ABB=ON  L34 OR L33
L36          2 SEA FILE=REGISTRY ABB=ON  (AVIDIN OR BIOTIN)/CN
L37          4 SEA FILE=HCAPLUS ABB=ON  L35 AND (?MICROTUBUL?(W)?MOTOR?(W)?PRO
               TEIN? OR L36 OR ?AVIDIN? OR ?BIOTIN? OR ?ANTI?(W)?TUBULIN(W)?AN
               TIBOD? OR ?MICROTUBUL?(W)?BIND?(W)?PROTEIN? OR MAP)
L39          1 SEA FILE=HCAPLUS ABB=ON  L35 AND (?POLYARGININE? OR ?POLYHISTID
               INE? OR ?POLYLYSINE?)
L40          1 SEA FILE=HCAPLUS ABB=ON  L35 AND ?CONTACT?(4A)(?TUBULIN? OR
               ?MICROTUBULE?)
L41         40 SEA FILE=HCAPLUS ABB=ON  L35 OR L37 OR L39 OR L40
L42         35 SEA FILE=HCAPLUS ABB=ON  L41 AND (PRD<20040120 OR PD<20040120)

L43          1 SEA FILE=HCAPLUS ABB=ON  L42 AND ?DEPOLYMERIZ?(4A)?INHIBIT?
L44         35 SEA FILE=HCAPLUS ABB=ON  L42 OR L43


=> d ibib abs l44 1-35

L44  ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:470355  HCAPLUS
DOCUMENT NUMBER:          144:463810
TITLE:                    Method for the detection of stress biomarkers
                          including cortisol by fluorescence polarization
INVENTOR(S):              Cullum, Malford E.; Duplessis, Christopher A.;
                          Crepeau, Loring J.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S.
                          Ser. No. 700,868.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006105397	A1	20060518	US 2006-328486	20060104 <--
US 2005095601	A1	20050505	US 2003-700868	20031105
AU 2003287153	A1	20050624	AU 2003-287153	20031105 <--
PRIORITY APPLN. INFO.:			US 2003-700868 A2	20031105 <--
			WO 2003-US32736 A	20031105 <--

AB The inventive subject matter relates to a competitive method measuring stress biomarkers in bodily fluids including serum, urine and oral fluids including saliva. The inventive method measures biomarkers including cortisol, melatonin and secretory IgA by fluorescence polarization, fluorescence lifetime anal. or fluorescence resonance energy transfer. Cortisol was determined in saliva samples by competitive fluorescence polarization immunoassay using fluorescein-labeled cortisol and antibodies specific to cortisol.

L44 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:517344 HCAPLUS
DOCUMENT NUMBER: 143:19937
TITLE: Double motor mutant assay utilizing microtubule-associated genes, for screening antifungal agents having antimitotic activity
INVENTOR(S): Roof, David M.; Maxon, Mary
PATENT ASSIGNEE(S): Cytokinetics, Inc., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6905840	B1	20050614	US 2003-414270	20030414 <--
PRIORITY APPLN. INFO.:			US 2003-414270	20030414 <--

AB This invention provides a method for identifying compds. with potential antifungal activity and, in particular, compds. which disrupt fungal mitosis by altering the stability of fungal microtubules. The method utilizes fungal double mutants having hyper-stable microtubules to screen for agents with microtubule-destabilizing activity. Fungal cells having double mutations which alter microtubule stability and inhibit cell proliferation are used in the methods. Such mutations are most preferably in fungal cells from Saccharomyces, Aspergillus, Histoplasma, Cryptococcus, or Candida. Double mutants of microtubule-associated genes, such as Kip3/Dyn1, Kip3/Kar3 or Dyn1/Kar3, were characterized, and synthetic lethality and functional overlap were demonstrated. **Test** compds. are screened to identify those which are able to promote cell proliferation of the mutant fungal cells and counteract the stabilizing effect of the double mutations on the microtubules. Proliferation of the mutant cells indicates that the **test** compound relieves the effects of the mutation and is a potential antifungal agent. High-throughput methods of selecting for the novel antifungal agents are also provided.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:394676 HCAPLUS
DOCUMENT NUMBER: 142:426350
TITLE: Detection and identification of biopolymers using

nanopores and fluorescence quenching
INVENTOR(S): Pittaro, Richard J.; Verdonk, Edward D.; Doherty, Thomas P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005095599	A1	20050505	US 2003-699478	20031030
WO 2005045392	A2	20050519	WO 2004-US26959	20040818 <--
WO 2005045392	A3	20060119		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1682673	A2	20060726	EP 2004-786536	20040818 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.:
US 2003-699478 A 20031030 <--
WO 2004-US26959 W 20040818

AB The present invention relates to detection and identification of biopolymers using nanopores and fluorescence quenching. The apparatus includes a substrate having a nanopore, at least one excitable mol. (such as quantum dots, ions, metals, **monomer**, atom, halide, amino acid, nucleotide, simple sugar, nanosphere) attached to the substrate adjacent to the nanopore, and a light source such as laser for exciting the excitable mol. attached to the substrate adjacent to the nanopore wherein the excitable mol. is quenched by the quencher mol. on the nanoscale moiety as it passes by the excitable mol. The invention also includes a method for detecting the presence or identity of the nanoscale moiety.

L44 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:260209 HCAPLUS
DOCUMENT NUMBER: 142:329802
TITLE: Tau factor with modified **tubulin**-binding repeat (TBR) associated with formation of tau aggregates, and engineering cellular and animal models of tauopathies for drug discovery
INVENTOR(S): Wouters, Fred S.; Iliev, Asparouh I.
PATENT ASSIGNEE(S): Georg-August-Universitaet Goettingen, Germany
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005026360	A1	20050324	WO 2004-EP10392	20040916 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1516930	A1	20050323	EP 2003-20506	20030916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
EP 1678304	A1	20060712	EP 2004-765292	20040916 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:
EP 2003-20506 A 20030916 <--
US 2003-503519P P 20030916 <--
WO 2004-EP10392 W 20040916

AB The present invention provides tau factor mutants with modified microtubule binding domains, which can be identified as a **tubulin** -binding repeats (TBRs), and which leads to formation of tau aggregates exhibiting the properties of neurofibrillary tangles (NFTs) when introduced into a cell. The invention further provides nucleic acid mols. encoding these tau factor mutants, cells comprising the polypeptides and transgenic animals with cells expressing these polypeptides. The polypeptides of the invention form the basis for animal and cellular models of tau pathol., which form the basis for mol. screens for biomols. involved in tauopathies, but also for medicaments useful for the treatment of tauopathies. Neurotoxicity of mutant tau in primary mouse neurons was demonstrated. Pathol. effects in transgenic Drosophila and mouse were evaluated. It was demonstrated prevention of pathol. effects in transgenic mice by vaccination.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:253295 HCAPLUS
DOCUMENT NUMBER: 142:309849
TITLE: Tau factor with modified **tubulin**-binding repeat (TBR) associated with formation of tau aggregates, and engineering cellular and animal models of tauopathies for drug discovery
INVENTOR(S): Wouters, Fred S.; Iliev, Asparouh I.
PATENT ASSIGNEE(S): Georg-August Universitaet Goettingen, Germany
SOURCE: Eur. Pat. Appl., 77 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1516930	A1	20050323	EP 2003-20506	20030916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

WO 2005026360 A1 20050324 WO 2004-EP10392 20040916 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1678304 A1 20060712 EP 2004-765292 20040916 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
PRIORITY APPLN. INFO.: EP 2003-20506 A 20030916 <--
US 2003-503519P P 20030916 <--
WO 2004-EP10392 W 20040916

AB The present invention provides tau factor mutants with modified microtubule binding domains, which can be identified as a **tubulin** -binding repeats (TBRs), and which leads to formation of tau aggregates exhibiting the properties of neurofibrillary tangles (NFTs) when introduced into a cell. The invention further provides nucleic acid mols. encoding these tau factor mutants, cells comprising the polypeptides and transgenic animals with cells expressing these polypeptides. The polypeptides of the invention form the basis for animal and cellular models of tau pathol., which form the basis for mol. screens for biomols. involved in tauopathies, but also for medicaments useful for the treatment of tauopathies.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:829524 HCAPLUS
DOCUMENT NUMBER: 141:421487
TITLE: Correct diffusion coefficients of proteins in fluorescence correlation spectroscopy. Application to **tubulin oligomers** induced by Mg2+ and paclitaxel
AUTHOR(S): Krouglova, Tatiana; Vercammen, Jo; Engelborghs, Yves
CORPORATE SOURCE: Laboratory of Biomolecular Dynamics, Katholieke Universiteit Leuven, Louvain, B-3001, Belg.
SOURCE: Biophysical Journal (**2004**), 87(4), 2635-2646
CODEN: BIOJAU; ISSN: 0006-3495
PUBLISHER: Biophysical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In view of recent warnings for artifacts in fluorescence correlation spectroscopy, the diffusion coefficient of a series of labeled proteins in a wide range of mol. mass (43-670 kDa) was determined and shown to be correct with respect to published values and the theory. Fluorescence correlation spectroscopy was then applied to the study of fluorescently labeled **tubulin** and its **oligomerization** in vitro induced by Mg2+ ions, paclitaxel, and a fluorescent derivative of paclitaxel (Flutax2). By applying relations derived from the theory of Oosawa, we were able to determine the association constant of the **oligomers** induced by Mg2+. With Flutax2 our expts. show that at nanomolar concentration, the fluorescent derivative is able to recruit **tubulin dimers** and to form **oligomers** of defined size. Flutax2 does not bind to microtubules

preformed with paclitaxel, but it becomes preferentially incorporated into microtubules when Flutax2 **oligomers** are preformed, and microtubule formation is induced by paclitaxel addition This shows that their incorporation into microtubules is faster than the displacement of the prebound drug. Expts. using fluorescently labeled **tubulin** and (unlabeled) paclitaxel confirm the induction of **tubulin** **oligomers** at limiting paclitaxel concns.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:311086 HCAPLUS
DOCUMENT NUMBER: 140:332440
TITLE: Fluorescence analysis-based method for screening modulators of mitochondrial function, and the modulators obtained
INVENTOR(S): Jacotot, Etienne; Lecoeur, Herve; Rebouillat, Dominique
PATENT ASSIGNEE(S): Theraptosis S.A., Fr.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031768	A2	20040415	WO 2003-EP12056	20031002 <--
WO 2004031768	A3	20050707		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2505132	AA	20040415	CA 2003-2505132	20031002 <--
AU 2003274095	A1	20040423	AU 2003-274095	20031002 <--
EP 1567857	A2	20050831	EP 2003-758082	20031002 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1720452	A	20060111	CN 2003-80104774	20031002 <--

PRIORITY APPLN. INFO.:			
US 2002-415092P	P	20021002	<--
US 2003-472725P	P	20030523	<--
WO 2003-EP12056	W	20031002	<--

AB The invention discloses a method for screening modulators of mitochondrial function comprising adding a compound to be **tested** in a purified, isolated mitochondria preparation and simultaneously using fluorimetric anal. of mitochondrial morphol., and especially real-time fluorimetric anal., combining anal. of morphometric parameters (SSC/FSC parameters) with anal. of membrane integrity by dye fluorescence. The invention has application to the obtaining of peptides which induce mitochondrial membrane permeabilization.

L44 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:259755 HCAPLUS

DOCUMENT NUMBER: 141:327853
TITLE: Fluorescence correlation spectroscopy investigation of a GFP mutant-enhanced cyan fluorescent protein and its **tubulin** fusion in living cells with two-photon excitation
AUTHOR(S): Wang, Zifu; Shah, Jagesh V.; Chen, Zhongping; Sun, Chung-Ho; Berns, Michael W.
CORPORATE SOURCE: Beckman Laser Institute, University of California at Irvine, Irvine, CA, 92612, USA
SOURCE: Journal of Biomedical Optics (**2004**), 9(2), 395-403
CODEN: JBOPFO; ISSN: 1083-3668
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigates the feasibility of using the enhanced cyan mutant of green fluorescent protein (ECFP) as a probe for two-photon fluorescence correlation spectroscopy (FCS). Mol. dynamics and other properties of ECFP and an ECFP-**tubulin** fusion protein were investigated in living Potorous tridactylis (PTK2) cells. ECFP has high mol. brightness in the nucleus (η=3.3 kcpsm) and in the cytoplasm (3.2 kcpsm) under our exptl. conditions. The diffusion consts. of ECFP were determined to be 20±7 μm2/s in the nucleus and 21±8 μm2/s in the cytoplasm. ECFP has stable mol. characteristics with negligible photobleaching and photodynamic effects in the authors' measurements. At the highest concentration of **monomer** ECFP (425 nM) the amount of **dimer** ECFP was estimated to be negligible (.apprx.1.8 nM), consistent with the authors' data anal. using a single species model. ECFP-**tubulin** has a diffusion constant of 6 μm2/s in the living cells. In addition, the authors demonstrate that anal. of the mol. brightness can provide a new avenue for studying the polymerization state of **tubulin.** The authors suggest that the **tubulin** in the vicinity of the nucleus exists primarily as a **heterodimer** subunit while those in the area away from the nucleus (d>5 μm) are mostly **oligomers.** The authors conclude that ECFP is a useful genetic fluorescent probe for FCS studies of various cellular processes when in fusion to other biomols. of interest.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:15108 HCAPLUS
DOCUMENT NUMBER: 140:72885
TITLE: **Tubulin** equilibrium unfolding followed by time-resolved fluorescence and fluorescence correlation spectroscopy
AUTHOR(S): Sanchez, Susana A.; Brunet, Juan E.; Jameson, David M.; Lagos, Rosalba; Monasterio, Octavio
CORPORATE SOURCE: Laboratory for Fluorescence Dynamics, Department of Physics, University of Illinois at Urbana-Champaign, Urbana, IL, 61801-3080, USA
SOURCE: Protein Science (**2004**), 13(1), 81-88
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pathway for the in vitro equilibrium unfolding of the **tubulin** (I) **heterodimer** by guanidinium chloride (GdmCl)was studied using several spectroscopic techniques, specifically CD, two-photon fluorescence correlation spectroscopy (FCS), and time-resolved fluorescence, including

lifetime and dynamic polarization. The results showed that I unfolding was characterized by distinct processes that occurred in different GdmCl concentration ranges. At 0-0.5M GdmCl, a slight alteration of the I **heterodimer** occurred, as evidenced by a small, but reproducible increase in the rotational correlation time of the protein and a sharp decrease in the secondary structure monitored by CD. In the range of 0.5-1.5M GdmCl, significant decreases in the steady-state anisotropy and average lifetime of the intrinsic Trp fluorescence occurred, as well as a decrease in the rotational correlation time, from 48 to 26 ns. In the same GdmCl range, the number of protein mols. (labeled with Alexa 488), as determined by 2-photon FCS measurements, increased by a factor of 2, indicating dissociation of the I **dimer** into **monomers.** At 1.5-4M GdmCl, these **monomers** unfolded, as evidenced by the continual decrease in Trp steady-state anisotropy, average lifetime, and rotational correlation time, concomitant with secondary structural changes. These results assisted in elucidating the unfolding pathway of the I **heterodimer** and demonstrated the value of FCS measurements in studies of **oligomeric** protein systems.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:721349 HCAPLUS
DOCUMENT NUMBER: 140:223101
TITLE: Fluorescence spectroscopy studies on micellization of poloxamer 407 solution
AUTHOR(S): Lee, Kayoung; Shin, Sang-Chul; Oh, Injoon
CORPORATE SOURCE: College of Pharmacy and Research Institute of Drug Development, Chonnam National University, S. Korea
SOURCE: Archives of Pharmacal Research (**2003**), 26(8), 653-658
CODEN: APHRDQ; ISSN: 0253-6269
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been reported that at low temperature region, poloxamers existed as a **monomer.** Upon warming, an equilibrium between unimers and micelles was established, and finally micelle aggregates were formed at higher temperature In this study, the fluorescence spectroscopy was used to study the micelle formation of the poloxamer 407 in aqueous solution The excitation and emission spectra of pyrene, a fluorescence probe, were measured as a function of the concentration of poloxamer 407 and temperature A blue shift in the emission spectrum and a red shift in the excitation spectrum were observed as pyrene transferred from an aqueous to a hydrophobic micellar environment. From the I1/I3 and I339/I333 results, critical micelle concentration (cmc) and critical micelle temperature (cmt) were determined Also, from the fluorescence spectra of the probe mols. such as 8-anilino-1-naphthalene sulfonic acid and 1-pyrenecarboxaldehyde, the blue shift of the λmax was observed These results suggest a decrease in the polarity of the microenvironment around probe because of micelle formation. The poloxamer 407 above cmc strongly complexed with hydrophobic fluorescent probes and the binding constant of complex increased with increasing the hydrophobicity of the probe.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:563680 HCAPLUS

DOCUMENT NUMBER: 140:267098
TITLE: Set of fluorochromophores in the wavelength range from 450 to 700 nm and suitable for labeling proteins and amino-modified DNA
AUTHOR(S): Wetzl, Bianca; Gruber, Michaela; Oswald, Bernhard; Durkop, Axel; Weidgans, Bernhard; Probst, Mario; Wolfbeis, Otto S.
CORPORATE SOURCE: Institute of Analytical Chemistry, Chemo- and Biosensors, University of Regensburg, Regensburg, D-93040, Germany
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (**2003**), 793(1), 83-92
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We describe the synthesis, purification, and spectral properties of new dyes and reactive labels. They absorb in the visible range between 450 and 700 nm and display anal. useful fluorescence. They were made amino-reactive by esterification with N-hydroxysuccinimide (NHS). The resulting oxysuccinimide (OSI) esters were covalently linked to the amino groups of human serum albumin (HSA) or certain DNA **oligomers.** Except for dyes 9 and 13, they contain one reactive group only in order to avoid cross linking of biomols. Labeling of amino-modified biomols. was performed by standard protocols, and the labeled proteins and oligonucleotides were separated from the unreacted dye by gel chromatog. using Sephadex G25 as the stationary phase in the case of proteins, and reversed-phase HPLC in the case of DNA **oligomers.** The dyes also have been used as donor-acceptor pairs in fluorescence energy transfer systems and in energy transfer cascades.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:472643 HCAPLUS
DOCUMENT NUMBER: 139:30801
TITLE: Assays and implements for determining and modulating heat shock protein 90 (HSP90) binding activity, and therapeutic use
INVENTOR(S): Kamal, Adeela; Burrows, Francis J.; Zhang, Lin; Boehm, Marcus F.
PATENT ASSIGNEE(S): Conforma Therapeutics Corporation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050295	A2	20030619	WO 2002-US39993	20021212 <--
WO 2003050295	A3	20050210		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2468202 AA 20030619 CA 2002-2468202 20021212 <--
AU 2002364566 A1 20030623 AU 2002-364566 20021212 <--
EP 1519735 A2 20050406 EP 2002-799944 20021212 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY, TR, BG, CZ, EE, SK
JP 2005520795 T2 20050714 JP 2003-551316 20021212 <--
CA 2474508 AA 20030814 CA 2003-2474508 20030210 <--
WO 2003066005 A2 20030814 WO 2003-US4283 20030210 <--
WO 2003066005 A3 20040610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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AU 2003217393 A1 20030902 AU 2003-217393 20030210 <--
EP 1472230 A2 20041103 EP 2003-713437 20030210 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005530689 T2 20051013 JP 2003-565431 20030210 <--
WO 2004054624 A1 20040701 WO 2003-US18776 20030612 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003303058 A1 20040709 AU 2003-303058 20030612 <--
EP 1581261 A1 20051005 EP 2003-741983 20030612 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2005074457 A1 20050407 US 2004-498926 20041025 <--
US 2005267122 A1 20051201 US 2005-503880 20050222 <--
PRIORITY APPLN. INFO.: US 2001-340762P P 20011212 <--
US 2002-355275P P 20020208 <--
US 2002-367055P P 20020322 <--
WO 2002-US39993 W 20021212 <--
WO 2003-US4283 W 20030210 <--
WO 2003-US18776 W 20030612 <--

OTHER SOURCE(S): CASREACT 139:30801

AB Ligand binding assays as applied to HSP90s as receptors or ligands, and reagents useful therefore, are described and claimed, as are methods of assaying for HSP90 modulators and methods of using the resulting products identified thereby. The methodol. of the invention may be used in the treatment and prevention of an HSP90-mediated disease, e.g. cancer. Modulators of the invention include e.g. ansamycins.

L44 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:133452 HCAPLUS
DOCUMENT NUMBER: 138:183489
TITLE: Fluorescent assay for polymerization of purified bacterial FtsZ cell-division protein and use thereof in screening for FtsZ inhibitors as antibacterial agents
INVENTOR(S): Trusca, Dorina
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003014343	A1	20030220	WO 2002-US27119		20020806 <--
W: CA, JP, US					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR					
US 2004161793	A1	20040819	US 2004-483300		20040108 <--
PRIORITY APPLN. INFO.:			US 2001-311409P	P	20010810 <--
			WO 2002-US27119	W	20020806 <--

AB A method for identifying chemical inhibitors of FtsZ polymerization using a direct fluorescence detection technique. FtsZ is a **tubulin**-like FtsZ division protein localizes to the division site and serves a cytoskeletal role during septum formation. The disclosed novel fluorescent-based 96-well format filter assay developed to measure the polymerization of FtsZ comprises a mixture of **monomers** and aggregates (38 to .apprx.210 KDa in range) of purified wild-type FtsZ and a fluorescently tagged derivative of FtsZ protein (mutant FtsZT65C) in stoichiometric ratio, which is passed through a 0.2-μm filter membrane, while polymerized FtsZ is retained on the filter. Addition of the SulA protein to the assay leads to rapid disassembly of existing FtsZ polymers, demonstrating its natural regulatory effect on FtsZ under the assay conditions. This assay is sensitive (requiring 2 μM FtsZ or less) and facilitates high-throughput screening of factors affecting FtsZ polymerization The technique is based on the phys. separation of fluorescently-labeled polymers of FtsZ from **monomeric** forms. This invention has both research and clin. applications in the identification of inhibitors of FtsZ polymerization as potential antibacterial agents.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:32882 HCAPLUS
DOCUMENT NUMBER: 138:147344
TITLE: Stability of Drug-Induced **Tubulin** Rings by Fluorescence Correlation Spectroscopy
AUTHOR(S): Boukari, Hacene; Nossal, Ralph; Sackett, Dan L.
CORPORATE SOURCE: Laboratory of Integrative and Medical Biophysics, National Institutes of Health, National Institute of Child Health and Human Development, Bethesda, MD, 20892, USA
SOURCE: Biochemistry (**2003**), 42(5), 1292-1300
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fluorescence correlation spectroscopy (FCS) was applied to investigate the stability of **tubulin** rings that result from the interaction of αβ- **tubulin dimers** with three vinca domain-binding peptides-cryptophycin 1, hemiasterlin, and dolastatin 10. These peptides inhibit **tubulin** polymerization into microtubules and, instead, induce the formation of single-walled **tubulin** rings of 23.8 nm mean diameter for cryptophycin and 44.6 nm mean diameter for hemiasterlin and dolastatin, as revealed by electron microscopy on micromolar drug-**tubulin** samples. However, the hydrodynamic diameter and the apparent number of fluorescent particles, determined from anal. of FCS measurements obtained from nanomolar drug-**tubulin** samples, indicate variation in the stability of the rings depending on the drug and the **tubulin** concentration Cryptophycin-**tubulin** rings appear to be the most stable even with **tubulin** concentration as low as 1 nM, whereas hemiasterlin-**tubulin** rings are the least, depolymg. even at relatively high concns. (100 nM). In contrast, the dolastatin-**tubulin** rings demonstrate an intermediate level of stability, depolymg. significantly only at **tubulin** concns. below 10 nM. We also compare the stability results with those of cytotoxicity measurements taken on several cell lines and note a rough correlation between the cytotoxicity of the drugs in cell cultures and the stability of the corresponding drug-induced rings.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:6096 HCAPLUS
DOCUMENT NUMBER: 138:49893
TITLE: Protein aggregation assays and use in identification of therapeutic agents
INVENTOR(S): Kondejewski, Les; Chakrabartty, Avijit; Qi, Xiao-Fei; Cashman, Neil
PATENT ASSIGNEE(S): Caprion Pharmaceuticals Inc., Can.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000853	A2	20030103	WO 2002-US19836	20020620 <--
WO 2003000853	A3	20031204		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002310497	A1	20030108	AU 2002-310497	20020620 <--
US 2003022243	A1	20030130	US 2002-176809	20020620 <--
PRIORITY APPLN. INFO.:			US 2001-299849P P	20010620 <--

WO 2002-US19836 W 20020620 <--

AB The invention features methods for identifying agents that modulate protein aggregation or stabilize protein conformation. The methods include an in vitro aggregation assay, a native state stabilization assay, a cell-based screening assay, and an animal-based screening assay. These methods can be used to identify agents useful for the treatment of conformational diseases resulting from aggregation of a protein.

L44 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:649824 HCAPLUS
DOCUMENT NUMBER: 137:365767
TITLE: Fluorescent assay for polymerization of purified bacterial FtsZ cell-division protein
AUTHOR(S): Trusca, Dorina; Bramhill, David
CORPORATE SOURCE: Biologics Research, Department of Endocrinology and Chemical Biology, Merck Research Laboratories, Rahway, NJ, 07065-0900, USA
SOURCE: Analytical Biochemistry (**2002**), 307(2), 322-329
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Septum formation in Escherichia coli is a complex cascade of interactions among cell-division proteins. The **tubulin**-like FtsZ division protein localizes to the division site and serves a cytoskeletal role during septum formation. A novel fluorescent-based 96-well format filter assay has been developed to measure the polymerization of FtsZ. A mixture of **monomers** and aggregates (38 to .apprx.200 KDa in range) of purified wild-type FtsZ and a fluorescently tagged derivative of FtsZ protein in stoichiometric ratio passes through a 0.2-μm filter membrane, while polymerized FtsZ is retained on the filter. Addition of the SulA protein to the assay leads to rapid disassembly of existing FtsZ polymers, demonstrating its natural regulatory effect on FtsZ under the assay conditions. This assay is sensitive (requiring 2 μM FtsZ or less) and facilitates high-throughput screening of factors affecting FtsZ polymerization
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:314203 HCAPLUS
DOCUMENT NUMBER: 138:69258
TITLE: Effect of urea denaturation on tryptophan fluorescence and nucleotide binding on **tubulin** studied by fluorescence and NMR spectroscopic methods
AUTHOR(S): Kuchroo, K.; Maity, H.; Kasturi, S. R.
CORPORATE SOURCE: Department of Chemical Sciences, Tata Institute of Fundamental Research, Mumbai, 400 005, India
SOURCE: Physiological Chemistry and Physics and Medical NMR (**2001**), 33(2), 139-151
CODEN: PCPNER; ISSN: 0748-6642
PUBLISHER: Pacific Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Tubulin**, the major protein of microtubules, has been shown to be an example of a protein undergoing multistep unfolding. Local unfolding and stepwise loss of a number of characteristic functions were demonstrated. In order to understand urea induced effects on tryptophan fluorescence and nucleotide binding on **tubulin**, both fluorescence and NMR

techniques were used. **Tubulin** was denatured by different urea concns. The present expts. were carried out at concns. of **tubulin** (.apprx.10 μM) at which most of the protein will be in the **dimeric** state. Quenching studies in the presence of KI suggest that all the tryptophans are fairly solvent exposed. Similar studies using acrylamide as quencher, suggest unfolding of **tubulin** at these protein concns. to be an apparent two state process between the native and the completely unfolded states unlike at low concns. where a partially folded intermediate was observed No observable effects of the nucleotide or the metal ion on tryptophan fluorescence were observed An attempt was made using NMR to monitor the changes in the nucleotide interaction with **tubulin** as the protein is unfolded by urea denaturation. No significant effects were observed in the binding of the nucleotide to **tubulin** by urea denaturation.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:851181 HCAPLUS
DOCUMENT NUMBER: 135:366718
TITLE: Method of identifying critical points within protein-protein interactions
INVENTOR(S): Prusiner, Stanley B.; Cohen, Fred E.; James, Thomas L.; Kaneko, Kiyotoshi
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087911	A1	20011122	WO 2001-US15832	20010515 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001061671	A5	20011126	AU 2001-61671	20010515 <--
EP 1290004	A1	20030312	EP 2001-935592	20010515 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-572980 A 20000516 <--
WO 2001-US15832 W 20010515 <--

AB A method is disclosed for identifying compound defined by pharmacophores which compound affect protein-protein interactions. The method involves determining functional residues of at least one protein of a protein-protein interaction of interest. Three-dimensional structures are then developed based on the positions of the functional residues. The three-dimensional structures are then compared against compds. which have calculatable tertiary structures to identify compds. having a spatial orientation consistent with functionally relevant portions of a protein of the protein-protein interaction of interest. The method is applied to prion proteins and the search for the treatment of prion diseases. Dominant

neg. mutations in a PrP gene are described which result in inhibition of prion formation. Understanding information regarding these mutations results in (1) improving rational drug design technol. thereby providing drugs which inhibit prion formation; and (2) improving gene therapy technologies making it possible to produce genes which can produce prion resistant livestock. The drugs and the proteins of the mutated genes have similarity in their 3-dimensional shapes which result in similar physiol. characteristics in terms of inhibiting prion formation. A method of identifying compds. which affect protein-protein interactions is disclosed. The process can be supplemented by (1) creating transgenic animals which express or **test** variants; and/or (2) using a computer program to determine small mols. which would be the best candidates for having a desired effect on the protein-protein interaction of interest. Mols. are disclosed that interact with the cellular components involved in conversion of PrPC to PrPSc. The mols. disclosed can be small mols., peptides or protein analogs, e.g. analogs of PrPC. In one embodiment, these mols. interfere with prion formation and/or replication, e.g. by preventing interactions of proteins involved in a prion complex or by interfering with β-sheet formation. In another embodiment, the mols. of the invention promote PrPc conversion to PrPSc, e.g. by binding to PrPC and facilitating a conformational change from PrPC to PrPSc. The mols. may be designed to be species specific, meaning that the mol. will only bind to PrPC or Prion Protein Modulator Factor (PPMF) of the same or a genetically similar species. The presence of PPMF is needed to convert PrPC to PrPSc.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:693351 HCAPLUS
DOCUMENT NUMBER: 135:221256
TITLE: Fluorescence correlation spectroscopy for the screening of substances that influence cellular processes
INVENTOR(S): Bohnert, Georg; Camacho-Gomez, Juan; Kirschstein, Omar Steffen; Kittler, Leonhard; Neumann, Tobias; Unger, Eberhard
PATENT ASSIGNEE(S): Carl Zeiss Jena G.m.b.H., Germany
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068680	A2	20010920	WO 2001-EP2922	20010315 <--
WO 2001068680	A3	20020822		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10013854	A1	20010920	DE 2000-10013854	20000317 <--
EP 1264178	A2	20021211	EP 2001-925461	20010315 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004023228	A1	20040205	US 2003-221953	20030509 <--
PRIORITY APPLN. INFO.:			DE 2000-10013854 A	20000317 <--
			WO 2001-EP2922 W	20010315 <--

AB The invention concerns a fluorescence correlation spectroscopic method and

device for the determination of protein self assembly in the presence of active substances by measuring two fluorescence signals: the first signal is measured at self association equilibrium in the presences of the active substance and fluorescence labeled **monomers** and **dimers**; the second signal is captured at equilibrium state without adding the active substance. Associating proteins are **tubulins**, F-actins, Tau proteins; active substance are e.g. paclitaxel, nocodazole, vinblastine, colchicine.

L44 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:380005 HCAPLUS
DOCUMENT NUMBER: 135:16241
TITLE: Determination of the net exchange rate of **tubulin dimer** in steady-state microtubules by fluorescence correlation spectroscopy
AUTHOR(S): Neumann, Tobias; Kirschstein, Steffen O.; Gomez, Juan A. Camacho; Kittler, Leonhard; Unger, Eberhard
CORPORATE SOURCE: Institut fur Molekulare Biotechnologie e. V. Jena, Jena, D-07745, Germany
SOURCE: Biological Chemistry (**2001**), 382(3), 387-391
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The microtubule cytoskeleton plays an important role in eukaryotic cells, e.g., in cell movement or morphogenesis. Microtubules, formed by assembly of **tubulin dimers**, are dynamic polymers changing randomly between periods of growing and shortening, a property known as dynamic instability. Another process characterizing the dynamic behavior is the so-called treadmilling due to different binding consts. of **tubulin** at both microtubule ends. In this study, we used tetramethylrhodamine (TMR)-labeled **tubulin** added to microtubule suspensions to determine the net exchange rate (NER) of **tubulin dimers** by fluorescence correlation spectroscopy (FCS) as a measure for microtubule dynamics. This approach, which seems to be suitable as a screening system to detect compds. influencing the NER of **tubulin dimers** into microtubules at steady-state, showed that taxol, nocodazole, colchicine, and vinblastine affect microtubule dynamics at concns. as low as 10-9-10-10 M.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:292691 HCAPLUS
DOCUMENT NUMBER: 135:89447
TITLE: The ligand affinity of proteins measured by isothermal denaturation kinetics
AUTHOR(S): Epps, Dennis E.; Sarver, Ronald W.; Rogers, Joseph M.; Herberg, John T.; Tomich, Paul K.
CORPORATE SOURCE: Pharmacia Corporation, Kalamazoo, MI, 49001, USA
SOURCE: Analytical Biochemistry (**2001**), 292(1), 40-50
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An isothermal denaturation kinetic method was developed for identifying potential ligands of proteins and measuring their affinity. The method is suitable for finding ligands specific toward proteins of unknown function

and for large-scale **drug screening.** It consists of analyzing the kinetics of isothermal denaturation of the protein-with and without the presence of potential specific ligands-as measured by long-wavelength fluorescent dyes whose quantum yield increases when bound to hydrophobic regions exposed upon unfolding of the proteins. The exptl. procedure was developed using thymidylate kinase and stromelysin as target proteins. The kinetics of thermal unfolding of both of these enzymes were consistent with a pathway of two consecutive first-order rate-limiting steps. Reflecting the stabilizing effect of protein/ligand complexes, the presence of specific ligands decreased the value of the rate consts. of both steps in a dose-dependent manner. The dependence of the rate consts. on ligand concentration obeyed a simple binding isotherm, the anal. of which yielded an accurate equilibrium constant for ligand binding. The method was validated by comparing its results with those obtained under the same conditions by steady-state fluorescence spectroscopy, CD, and uv spectrophotometry: The corresponding rate consts. were comparable for each of the anal. detection methods. (c) 2001 Academic Press.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:185957 HCAPLUS
DOCUMENT NUMBER: 134:234015
TITLE: Nucleic acid sequence analysis by measurement of interaction of individual bases with fluorescent moieties
INVENTOR(S): Russell, Terence S.
PATENT ASSIGNEE(S): Lifebeam Technologies, Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001018247	A2	20010315	WO 2000-US24140		20000901 <--
WO 2001018247	A3	20020103			
W: AU, CA, CN, JP, RU					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 6528258	B1	20030304	US 2000-653046		20000901 <--
PRIORITY APPLN. INFO.:			US 1999-152465P	P	19990903 <--
			US 1999-158703P	P	19991008 <--

AB A high speed method for sequencing of large DNA mols. is described. The method involves directly measuring the interaction individual bases in the nucleic acid and a fluorescent reporter moiety. By measuring the effects of the interaction between the fluorescent group and the bases on the fluorescence, the individual bases can be identified. Different fluorescent groups with different behaviors to different bases may be used in combination to increase the accuracy of base-calling. The apparatus organizes the nucleic acids for scanning by drawing them electrophoretically through pores in membranes formed by pore-forming proteins such as porins or hemolysins. The protein may be modified by an amino acid substitution that allows a fluorescent group to be incorporated near the pore. Mixed **oligomers** containing only one fluorescent group per pore complex are prepared by controlling the mixing ratio of the two types of subunit.

L44 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:911534 HCAPLUS
DOCUMENT NUMBER: 134:66121
TITLE: Compositions and methods for assaying subcellular conditions and processes using energy transfer for **drug screening**
INVENTOR(S): Dykens, James A.; Velicelebi, Gonul; Ghosh, Soumitra S.
PATENT ASSIGNEE(S): Mitokor, USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000079274	A2	20001228	WO 2000-US17380	20000622 <--
WO 2000079274	A3	20020110		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6323039	B1	20011127	US 1999-338122	19990622 <--
US 6280981	B1	20010828	US 2000-514569	20000223 <--
CA 2375542	AA	20001228	CA 2000-2375542	20000622 <--
EP 1210596	A2	20020605	EP 2000-943119	20000622 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506014	T2	20030218	JP 2001-505191	20000622 <--

PRIORITY APPLN. INFO.:			
US 1999-140433P	P	19990622	<--
US 1999-338122	A	19990622	<--
US 2000-176383P	P	20000114	<--
WO 2000-US17380	W	20000622	<--

AB The invention provides compns. and methods for monitoring subcellular compartments such as organelles by energy transfer techniques that do not require specific intermol. affinity binding events between energy transfer donor and energy transfer acceptor mols. pH. Provided are methods for assaying cellular membrane potential, including mitochondrial membrane potential, by energy transfer methodologies including fluorescence resonance energy transfer (FRET). Diagnostic and **drug screening** assays are also provided.

L44 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:227858 HCAPLUS
DOCUMENT NUMBER: 132:260666
TITLE: Identifying agents that alter mitochondrial permeability transition pores and cell death for diagnostic and therapeutic use
INVENTOR(S): Dykens, James A.; Miller, Scott W.; Ghosh, Soumitra S.; Davis, Robert E.
PATENT ASSIGNEE(S): Mitokor, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000019200	A1	20000406	WO 1999-US22261	19990924 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003044776	A1	20030306	US 1998-161172	19980925 <--
CA 2345066	AA	20000406	CA 1999-2345066	19990924 <--
AU 9961628	A1	20000417	AU 1999-61628	19990924 <--
EP 1116027	A1	20010718	EP 1999-948458	19990924 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525630	T2	20020813	JP 2000-572655	19990924 <--
PRIORITY APPLN. INFO.:			US 1998-161172 A	19980925 <--
			WO 1999-US22261 W	19990924 <--

AB Methods are provided for identifying agents that affect mitochondrial functions and cell death. Such agents are useful for treating diseases associated with mitochondrial dysfunction and in methods of identifying a risk or presence of such diseases. In particular, the invention relates to the loss of mitochondrial membrane potential ($\Delta\Psi m$) during mitochondrial permeability transition (MPT) and further provides a measurable rate loss function, changes in which are useful e.g. for detecting agents that affect one or more mitochondrial functions, for detecting mitochondrial diseases, and for studying mol. components of mitochondria that regulate MPT.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:210502 HCAPLUS
DOCUMENT NUMBER: 132:231929
TITLE: Method and apparatus for cell-based **drug screening**
INVENTOR(S): Dunlay, R. Terry; Taylor, D. Lansing; Gough, Albert H.; Guiliano, Kenneth A.; Rubin, Richard A.
PATENT ASSIGNEE(S): Cellomics, Inc., USA
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017643	A2	20000330	WO 1999-US21561	19990917 <--
WO 2000017643	A3	20001012		
W: AU, CA, JP, MX, NZ, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				

PT, SE
CA 2344567 AA 20000330 CA 1999-2344567 19990917 <--
AU 9960485 A1 20000410 AU 1999-60485 19990917 <--
EP 1114320 A2 20010711 EP 1999-969495 19990917 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002525603 T2 20020813 JP 2000-571253 19990917 <--
PRIORITY APPLN. INFO.: US 1998-100973P P 19980918 <--
WO 1999-US21561 W 19990917 <--

AB The invention concerns a high throughput screening method to identify compds. that modify transcription factor activation and/or protein kinase activation by contacting cells that contain fluorescent labeled transcription factors/protein kinases with the **test** compound and detecting the distribution of the labeled compound between cell nucleus and cytoplasm using an automated analyzer. The present invention provides systems, methods, screens, and kits for optical system anal. of cells to rapidly determine the distribution, environment, or activity of fluorescently labeled reporter mols. in cells for the purpose of screening large nos. of compds. for those that specifically affect particular biol. functions. The invention involves providing cells containing fluorescent reporter mols. in an array of locations and scanning numerous cells in each location with a high magnification fluorescence optical system, converting the optical information into digital data, and utilizing the digital data to determine the distribution, environment or activity of the fluorescently labeled reporter mols. in the cells. The array of locations may be an industry standard 96 well or 384 well microtiter plate or a microplate which is a microplate having cells in a micropatterned array of locations. The invention includes apparatus and computerized method for processing, displaying and storing the data.

L44 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:101698 HCAPLUS
DOCUMENT NUMBER: 133:37651
TITLE: High throughput screening with multiphoton excitation
AUTHOR(S): Lakowicz, Joseph R.; Gryczynski, Ignacy; Gryczynski, Zygmunt
CORPORATE SOURCE: School of Medicine, University of Maryland, Baltimore, MD, USA
SOURCE: Journal of Biomolecular Screening (**1999**), 4(6), 355-361
CODEN: JBISF3; ISSN: 1087-0571
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fluorescence detection is extensively used in high throughput screening. In HTS there is a continuous migration toward higher d. plates and smaller sample vols. In the present report the authors describe the advantages of two-photon or multiphoton excitation for HTS. Multiphoton excitation (MPE) is the simultaneous absorption of two long-wavelength photons to excite the lowest singlet state of the fluorophore. MPE is typically accomplished with short but high-intensity laser pulses, which allows simultaneous absorption of two or more photons. The intensity of the multiphoton-induced fluorescence is proportional to the square, cube, or higher power of the instantaneous photon flux. Consequently, two-photon or multiphoton excitation only occurs at the focal point of the incident beam. This property of two-photon excitation allows the excited volume to be very small and to be localized in the center of each well in the HTS plate. The authors show that two-photon-induced fluorescence of fluorescein can be reliably measured in microwell plates. The authors also show the use of 6-carboxy fluorescein as a pH probe with two-photon

excitation, and measure 4'-6-diamidino-2-phenylindole (**DAPI**) binding and two-photon-induced fluorescence. In further studies the authors measure the time-dependent intensity decays of **DAPI** bound to DNA and of calcium-dependent fluorophores. Finally, the authors demonstrate the possibility of three-photon excitation of several fluorophores, including indole, in the HTS plate. These results suggest that MPE can be used in high-d. multiwell plates.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:807509 HCAPLUS
DOCUMENT NUMBER: 132:146083
TITLE: Equilibrium Studies of a Fluorescent Paclitaxel Derivative Binding to Microtubules
AUTHOR(S): Li, Yankun; Edsall, Richard Jr.; Jagtap, Prakash G.; Kingston, David G. I.; Bane, Susan
CORPORATE SOURCE: Department of Chemistry, State University of New York at Binghamton, Binghamton, NY, 13902, USA
SOURCE: Biochemistry (**2000**), 39(3), 616-623
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A fluorescent derivative of paclitaxel, 3'-N-m-aminobenzamido-3'-N-debenzamidopaclitaxel (N-AB-PT), has been prepared to probe paclitaxel-microtubule interactions. Fluorescence spectroscopy was used to quant. assess the association of N-AB-PT with microtubules. N-AB-PT was found equipotent with paclitaxel in promoting microtubule polymerization Paclitaxel and N-AB-PT underwent rapid exchange with each other on microtubules assembled from GTP-, GDP-, and GMPCPP-**tubulin.** The equilibrium binding parameters for N-AB-PT to microtubules assembled from GTP-**tubulin** were derived through fluorescence titration N-AB-PT bound to two types of sites on microtubules (Kd1 = 61±7.0 nM and Kd2 = 3.3±0.54 μM). The stoichiometry of each site was less than one ligand per **tubulin dimer** in the microtubule (n1 = 0.81±0.03 and n2 = 0.44±0.02). The binding expts. were repeated after exchanging the GTP for GDP or for GMPCPP. It was found that N-AB-PT bound to a single site on microtubules assembled from GDP-**tubulin** with a dissociation constant of 2.5±0.29 μM, and that N-AB-PT bound to a single site on microtubules assembled from GMPCPP-**tubulin** with a dissociation constant of 15±4.0 nM. It therefore appears that microtubules contain two types of binding sites for paclitaxel and that the binding site affinity for paclitaxel depends on the nucleotide content of **tubulin.** It has been established that paclitaxel binding does not inhibit GTP hydrolysis and microtubules assembled from GTP-**tubulin** in the presence of paclitaxel contain almost exclusively GDP at the E-site. We propose that although all the subunits of the microtubule at steady state are the same "GDP-**tubulin**-paclitaxel", they are formed through two paths: paclitaxel binding to a **tubulin** subunit before its E-site GTP hydrolysis is of high affinity, and paclitaxel binding to a **tubulin** subunit containing hydrolyzed GDP at its E-site is of low affinity.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:673147 HCAPLUS
DOCUMENT NUMBER: 131:308619
TITLE: Assays for the detection of microtubule

depolymerization inhibitors
INVENTOR(S): Vale, Ronald D.; Hartman, James J.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953295	A1	19991021	WO 1999-US8086	19990413 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937457	A1	19991101	AU 1999-37457	19990413 <--
EP 1071943	A1	20010131	EP 1999-919826	19990413 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6410687	B1	20020625	US 1999-291170	19990413 <--
JP 2002522747	T2	20020723	JP 2000-543811	19990413 <--
US 6429304	B1	20020806	US 2000-724884	20001128 <--
US 6699969	B1	20040302	US 2000-724592	20001128 <--
US 6872537	B1	20050329	US 2000-673222	20001204 <--
US 2004161784	A1	20040819	US 2004-761781	20040120 <--
US 2005164230	A1	20050728	US 2004-927588	20040825 <--

PRIORITY APPLN. INFO.:

US 1998-81734P	P	19980414 <--
US 1999-291170	A3	19990413 <--
WO 1999-US8086	W	19990413 <--
US 2000-673322	A1	20001013 <--
US 2000-673222	A1	20001204 <--

AB This invention provides methods for the screening and identification of agents having potent effects on the progression of the cell cycle. In one embodiment, the methods involve **contacting** a polymerized **microtubule** with a **microtubule severing** protein or a **microtubule** depolymg. protein in the presence of an ATP or a GTP and a **test** agent; and (ii) detecting the formation of **tubulin monomers, dimers** or **oligomers.** The p60 subunit of katanin provides a particularly preferred **microtubule severing** protein possessing both ATPase and **microtubule severing** activities.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:331666 HCAPLUS
DOCUMENT NUMBER: 129:38321
TITLE: Separation of **Tubulin** Subunits under Nondenaturing Conditions
AUTHOR(S): Giraudel, Anne; Lafanechere, Laurence; Ronjat, Michel; Wehland, Juergen; Garel, Jean-Renaud; Wilson, Leslie; Job, Didier
CORPORATE SOURCE: Departement de Biologie Moleculaire et Structurale

CEA-Laboratoire du Cytosquelette, Institut National de la Sante et de la Recherche Medicale Unite n° 366 Commissariat a l'Energie Atomique, Grenoble, 38054, Fr.
SOURCE: Biochemistry (**1998**), 37(24), 8724-8734
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The dissociation and separation of the **tubulin** α- and β-subunits have been achieved by binding α-subunits to an immunoadsorbent gel and selectively inducing release of free β-subunits. The immunoadsorbent gel was prepared by coupling the monoclonal antibody YL1/2 to Sepharose 4B which specifically recognizes the C-terminal end of tyrosinated α-subunits. Extensive **tubulin** subunit dissociation and separation occurred in Tris buffer at neutral pH but was greatly enhanced at basic pHs (8.0-8.5). The binding of colchicine to **heterodimeric tubulin** resulted in a marked protection against dissociation The dissociation of **tubulin** subunits was accompanied by loss of colchicine binding capacity, and ability to polymerize into microtubules. As shown by CD, loss of functional properties was not due to extensive denaturation of **tubulin**, as **tubulin** retained most of its secondary structure. Neither of the separated α- or β-subunits was able to bind colchicine, but functional **tubulin** that was able to bind colchicine could be reconstituted from the dissociated subunits by changing the buffer to a neutral mixture of Tris and Pipes. The yield of reconstitution, as estimated from kinetic measurements of colchicine binding capacity, amounted to about 25%. Such a yield can probably be improved with minor changes in exptl. conditions. The quant. dissociation of **tubulin** into separated "native" α- and β-subunits should provide a powerful tool for further studies on the properties of the individual **tubulin** subunits and the structure-function relationships of the **tubulins.**
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:252521 HCAPLUS
DOCUMENT NUMBER: 129:38050
TITLE: Refolding of recombinant sulfonated procathepsin S and of reduced chicken cystatin; implications for renaturation experiments
AUTHOR(S): Zerovnik, Eva; Kopitar, Gregor; Kos, Janko; Turk, Vito
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, J. Stefan Institute, Ljubljana, 1001, Slovenia
SOURCE: Biochimica et Biophysica Acta, Protein Structure and Molecular Enzymology (**1998**), 1383(2), 211-218
CODEN: BBAEDZ; ISSN: 0167-4838
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Kinetic stopped-flow measurements of refolding of the recombinant sulfonated procathepsin S from 6 M urea are presented. The expts. were performed using intrinsic tryptophan fluorescence and fluorescence of the hydrophobic probe 1-anilino-naphthalene-8-sulfonate (**ANS**). Initially, ($t_{1/2}$=3±1 ms) an intermediate with increased **ANS** fluorescence and protected tryptophan environment is formed. Much later, a slow increase in **ANS** fluorescence occurs with no accompanying

changes in tryptophan fluorescence. The reaction of the slow **ANS** fluorescence increase correlates with the rate of aggregation as shown by the size exclusion chromatog. (SEC). For comparison, the folding reactions of the reduced chicken cystatin were measured, both, by intrinsic tryptophan and extrinsic **ANS** fluorescence. An early intermediate forms very fast in the refolding of reduced chicken cystatin on 6-fold dilution from 5.7 M GuHCl ($t_{1/2}$=5±2 ms), similarly to that observed for the sulfonated procathepsin S. **ANS** fluorescence and tryptophan fluorescence decrease further ($t_{1/2}$=100±50 ms) leading to a late, 'more structured' intermediate which is prone to **dimerization.**

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:78117 HCAPLUS
DOCUMENT NUMBER: 128:215136
TITLE: Binding of double-stranded DNA by Escherichia coli RecA protein monitored by a fluorescent dye displacement assay
AUTHOR(S): Zaitsev, Eugene N.; Kowalczykowski, Stephen C.
CORPORATE SOURCE: Division of Biological Sciences, Sections of Microbiology and Molecular and Cell Biology, University of California, Davis, CA, 95616-8665, USA
SOURCE: Nucleic Acids Research (**1998**), 26(2), 650-654
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have developed a new assay to characterize the double-stranded DNA (dsDNA) binding properties of RecA protein. This assay is based on measurement of changes in the fluorescence of a 4',6-diamidino-2-phenylindole (**DAPI**)-dsDNA complex upon RecA protein binding. The binding of RecA protein to a complex of **DAPI** and dsDNA results in displacement of the bound **DAPI**, producing a decrease in the observed fluorescence. **DAPI** displacement is dependent on both RecA protein and ATP; dATP and, to a lesser extent, UTP and dCTP also support the **DAPI** displacement reaction, but dGTP, GTP, dITP and TTP do not. Binding stoichiometry for the RecA protein-dsDNA complex measured by **DAPI** displacement is 3 bp per RecA protein **monomer** in the presence of ATP. These results, taken together with data for mutant RecA proteins, suggest that this **DAPI** displacement assay monitors formation of the high affinity DNA binding state of RecA protein. Since this state of RecA protein defines the form of the nucleoprotein filament that is active in DNA strand exchange, these findings raise the possibility that the RecA protein-dsDNA filament may possess a homologous pairing capacity.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:47022 HCAPLUS
DOCUMENT NUMBER: 128:190121
TITLE: Fluorescent taxoids as probes of the microtubule cytoskeleton
AUTHOR(S): Evangelio, Juan A.; Abal, Miguel; Barasoain, Isabel; Souto, Andre A.; Lillo, M. Pilar; Acuna, A. Ulises; Amat-Guerri, Francisco; Andreu, Jose M.
CORPORATE SOURCE: Centro de Investigaciones Biologicas, CSIC, Madrid,

28006, Spain
SOURCE: Cell Motility and the Cytoskeleton (**1998**), 39(1), 73-90
CODEN: CMCYEO; ISSN: 0886-1544
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Microtubules are specifically and efficiently visualized with the new fluorescent taxoids 7-O-[N-(4'-fluoresceincarbonyl)-L-alanyl]taxol (FLUTAX) and 7-O-[N-(4'-tetramethyl-rhodaminecarbonyl)-L-alanyl]taxol (ROTAX). Similarly to taxol, FLUTAX and ROTAX are able to drive inactive GDP-liganded **tubulin** into microtubule assembly. One mol. of FLUTAX binds per αβ- **tubulin dimer** assembled, competing with taxol for the same microtubule binding site with an eightfold smaller relative affinity. FLUTAX-induced microtubule elongation is markedly Mg2+-dependent, encompassing the binding of one Mg2+ ion more per **tubulin dimer** polymerized than in the case of taxol. A small perturbation of the absorption spectrum of bound FLUTAX is consistent with a cationic microenvironment relative to the solution The fluorescence anisotropy of FLUTAX increases by an order of magnitude upon binding to microtubules and time-resolved measurements indicate that the fluorescein moiety remains considerably mobile on a protein surface. The rate of labeling suggests that this is the outer microtubule wall. Alternatively, the microtubule lumen would be functional. FLUTAX- and ROTAX-induced microtubules, radial structures, and organized microtubule bundles are readily observed under the fluorescence microscope. Rapid and accurate visualization of native (or very mildly fixed) cytoplasmic and spindle microtubules of a variety of permeabilized cells is simply obtained with micromolar FLUTAX, with an advantage over immunofluorescence. In addition, FLUTAX labels the centrosomes of PtK2 cells more intensely than antibodies to α- or β- **tubulin**, and co-localizing with antibodies to γ- **tubulin.** Two brightly fluorescent spots, probably separating or duplicating centrioles, can be resolved in the centrosomes of interphase cells. This finding indicates that centrosomes may well be addnl. targets of action of taxoids. FLUTAX strongly labels microtubules near the spindle poles, as well as microtubules at the telophase spindle equator and the central part of the midbody in cytokinesis (instead of the dark zone frequently observed with immunofluorescence), suggesting a predominant interaction of FLUTAX with sites at which **tubulin** is newly polymerized Nanomolar concns. of FLUTAX also permit specific imaging of centrosomes, half-spindles and midbodies in growing U937 cells.
REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:746207 HCAPLUS
DOCUMENT NUMBER: 128:20302
TITLE: Microplate thermal shift assay and apparatus for ligand development and multi-variable protein chemistry optimization
INVENTOR(S): Pantoliano, Michael W.; Rhind, Alexander W.; Salemme, Francis R.; Springer, Barry A.; Bone, Roger F.; Petrella, Eugenio C.
PATENT ASSIGNEE(S): 3-Dimensional Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9742500	A1	19971113	WO 1997-US8154	19970509 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2253587	AA	19971113	CA 1997-2253587	19970509 <--
AU 9732050	A1	19971126	AU 1997-32050	19970509 <--
AU 741049	B2	20011122		
EP 914608	A1	19990512	EP 1997-927628	19970509 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6020141	A	20000201	US 1997-853464	19970509 <--
US 6036920	A	20000314	US 1997-853459	19970509 <--
NZ 332754	A	20000728	NZ 1997-332754	19970509 <--
JP 2000511629	T2	20000905	JP 1997-540260	19970509 <--
KR 2000011069	A	20000225	KR 1998-709222	19981109 <--
US 6291191	B1	20010918	US 1999-452203	19991202 <--
US 6232085	B1	20010515	US 1999-458691	19991210 <--
US 6268158	B1	20010731	US 1999-458663	19991210 <--
US 6214293	B1	20010410	US 1999-459996	19991214 <--
US 6268218	B1	20010731	US 1999-459997	19991214 <--
US 6291192	B1	20010918	US 2000-477724	20000105 <--
US 6303322	B1	20011016	US 2000-478216	20000105 <--
US 2002114734	A1	20020822	US 2001-801676	20010309 <--
US 6849458	B2	20050201		
US 2003203497	A1	20031030	US 2003-419973	20030422 <--
US 2004185504	A1	20040923	US 2004-821274	20040407 <--

PRIORITY APPLN. INFO.:	US 1996-17860P	P	19960509 <--
	US 1997-853459	A1	19970509 <--
	US 1997-853464	A1	19970509 <--
	WO 1997-US8154	W	19970509 <--
	US 1999-459996	A1	19991214 <--
	US 2001-801676	A1	20010309 <--

AB The present invention is a method for ranking the affinity of each of a multiplicity of different mols. for a target mol. which is capable of denaturing due to a thermal change. The method comprises contacting the target mol. with one mol. of the multiplicity of different mols. in each of a multiplicity of containers, simultaneously heating the multiplicity of containers, measuring in each of the containers a phys. change associated with the thermal denaturation of the target mol. resulting from the heating in each of the containers, generating a thermal denaturation curve for the target mol. as a function of temperature for each of the containers and determining a midpoint temperature (Tm) therefrom, comparing the Tm of each of the thermal denaturation curves with the Tm of a thermal denaturation curve obtained for the target mol. in the absence of any of the mols. in the multiplicity of different mols., and ranking the affinities of the multiplicity of different mols. according to the change in Tm of each of the thermal denaturation curves. The present invention also provides an assay apparatus that includes a temperature-adjusting means for simultaneously heating a plurality of samples, and a receiving means for receiving spectral emission from the samples while the samples are being heated. In

further aspects of the invention, the receiving means can be configured to receive fluorescent emission, UV light, and visible light. The receiving means can be configured to receive spectral emission from the samples in a variety of ways, e.g., one sample at a time, simultaneously from >1 sample, or simultaneously from all of the samples. The temperature-adjusting means can be configured with a temperature controller for changing temperature in accordance with a predetd. profile.

L44 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:601771 HCAPLUS
DOCUMENT NUMBER: 125:241775
TITLE: Method and kit for fluorometric analysis of enzymes catalyzing synthesis of nucleic acids
INVENTOR(S): Chavan, Surendra J.; Prochaska, Hans J.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9624694	A1	19960815	WO 1996-US1836		19960209	<--
W: AU, CA, JP, MX						
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
AU 9650225	A1	19960827	AU 1996-50225		19960209	<--
PRIORITY APPLN. INFO.:			US 1995-386469	A	19950210	<--
			WO 1996-US1836	W	19960209	<--

AB This invention provides a method for detecting in a sample an enzyme which catalyzes the synthesis of a double-stranded nucleic acid mol. from a nucleic acid template which comprises contacting the sample with a suitable fluorophore which selectively binds to double-stranded DNA. Also provided is a method for determining in a sample the activity of such an enzyme.
This invention also provides a method for detecting an RNA-DNA heteroduplex in a sample which comprises contacting the sample with a suitable fluorophore which selectively binds to double-stranded DNA. This method for detecting an RNA-DNA heteroduplex may further comprise quant. determining detected RNA-DNA heteroduplex. This invention also provides a method for detecting in a sample an enzyme that catalyzes the synthesis of an RNA-DNA heteroduplex from a nucleic acid template, as well as a method of detecting the activity of such an enzyme in a sample. This invention further provides a method for detecting the viral load of HIV in a sample. Also provided is a method for diagnosing an HIV infection in a subject, and for monitoring the progression of an HIV infection in a subject. Also provided is a method for determining the viral load of HIV in a subject infected with HIV. This invention further provides a method for identifying whether a substance inhibits reverse transcriptase. Finally, this invention provides a kit for assaying an enzyme which catalyzes the synthesis of a double-stranded nucleic acid mol. from a nucleic acid template.

L44 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:610287 HCAPLUS
DOCUMENT NUMBER: 103:210287
TITLE: A fluorometric assay for the **biotin**-

avidin interaction based on displacement of the fluorescent probe 2-anilinonaphthalene-6-sulfonic acid

AUTHOR(S): Mock, Donald M.; Langford, Gary; Dubois, Dwight; Criscimagna, Nick; Horowitz, Paul

CORPORATE SOURCE: Health Sci. Cent., Univ. Texas, San Antonio, TX, 78284, USA

SOURCE: Analytical Biochemistry (**1985**), 151(1), 178-81
CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Avidin** and **biotin** were sensitively and accurately quantitated using the fluorescent probe 2-anilinonaphthalene-6-sulfonic acid (2,6-**ANS**). In the presence of **avidin**, the fluorescence of 2,6-**ANS** is blue-shifted with a large increase in quantum yield. **Biotin** binding causes complete displacement of the bound fluorophore with concomitant quenching of the fluorescence. The fluorometric monitoring of the displacement of 2,6-**ANS** can be used as a facile method of measuring the **biotin-avidin** interaction. 2,6-**ANS** displacement gives the same stoichiometry as the method using 4'-hydroxyazobenzene-2-carboxylic acid. Initial studies of an affinity-purified **avidin** revealed that, of the 4 binding sites on the **avidin** tetramer, a mean of 3 remain available for **biotin** (or dye) binding; this finding highlights a caveat concerning the use of affinity-purified **oligomeric** -binding proteins with multiple sites. As compared with previous fluorescence methods, the use of 2,6-**ANS** gives high sensitivity without the necessity of preparing and purifying a covalent **avidin** conjugate. In addition, the present method is potentially more sensitive than those based on optical absorbance, uses a probe that has increased stability and a larger Stokes shift compared with fluorescein, is not subject to protein interference, and gives accurate results over a wide range of 2,6-**ANS** and **avidin** concns.

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=> d que stat l46
L5          1239 SEA FILE=REGISTRY ABB=ON  TUBULIN?/CN
L6             1 SEA FILE=REGISTRY ABB=ON  DAPI/CN
L7             2 SEA FILE=REGISTRY ABB=ON  ANS/CN
L8             1 SEA FILE=REGISTRY ABB=ON  82-76-8
L9             2 SEA FILE=REGISTRY ABB=ON  BIS-ANS/CN
L10            1 SEA FILE=REGISTRY ABB=ON  "NPN 3"/CN
L11            1 SEA FILE=REGISTRY ABB=ON  "NAPHTHYLENE DIISOCYANATE"/CN
L12            2 SEA FILE=REGISTRY ABB=ON  "RUTHENIUM RED"/CN
L13            1 SEA FILE=REGISTRY ABB=ON  DCVJ/CN
L14            1 SEA FILE=REGISTRY ABB=ON  "CRESOL FAST VIOLET"/CN
L15           11 SEA FILE=REGISTRY ABB=ON  L6 OR L7 OR L8 OR L9 OR L10 OR L11
                  OR L12 OR L13 OR L14
L16         1250 SEA FILE=REGISTRY ABB=ON  L15 OR L5
L29        31490 SEA FILE=HCAPLUS ABB=ON  L16 OR ?TUBULIN? OR ?DAPI? OR
                  ?ANILINONAPHTHALENE?(W)?SULFONATE? OR ANS OR BIS(W)ANS OR
                  BIS(W)?ANILINONAPHTHALENE?(W)?SULFONATE? OR N(W)PHENYL(W)1(W)?N
                  APHTHYLENE? OR NPN OR ?RUTHENIUM?(W)RED? OR ?CRESOL?(W)?VIOLET?
                   OR DCVJ OR ?JULOLIDINE?
L30          479 SEA FILE=HCAPLUS ABB=ON  L29 AND (?FLUOROMETRY? OR ?FLUORESENC?
                  )
L31           18 SEA FILE=HCAPLUS ABB=ON  L30 AND  DRUG(W)(SCREEN OR SCREENING)

L32           25 SEA FILE=HCAPLUS ABB=ON  L30 AND (?MONOMER? OR ?DIMER? OR
                  ?OLIGOMER? OR ?MICROTUBUL?(5A)?SEVER? OR ?TUBUL?(4A)?SEVER?)
L33           40 SEA FILE=HCAPLUS ABB=ON  L31 OR L32
L34            8 SEA FILE=HCAPLUS ABB=ON  L33 AND ?TEST?
L35           40 SEA FILE=HCAPLUS ABB=ON  L34 OR L33
L36            2 SEA FILE=REGISTRY ABB=ON  (AVIDIN OR BIOTIN)/CN
L37            4 SEA FILE=HCAPLUS ABB=ON  L35 AND (?MICROTUBUL?(W)?MOTOR?(W)?PRO
                  TEIN? OR L36 OR ?AVIDIN? OR ?BIOTIN? OR ?ANTI?(W)?TUBULIN(W)?AN
                  TIBOD? OR ?MICROTUBUL?(W)?BIND?(W)?PROTEIN? OR MAP)
L39            1 SEA FILE=HCAPLUS ABB=ON  L35 AND (?POLYARGININE? OR ?POLYHISTID
                  INE? OR ?POLYLYSINE?)
L40            1 SEA FILE=HCAPLUS ABB=ON  L35 AND ?CONTACT?(4A)(?TUBULIN? OR
                  ?MICROTUBULE?)
L41           40 SEA FILE=HCAPLUS ABB=ON  L35 OR L37 OR L39 OR L40
L45           34 SEA L41
L46           33 DUP REMOV L45 (1 DUPLICATE REMOVED)

=> d ibib abs l46 1-33

L46  ANSWER 1 OF 33  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
ACCESSION NUMBER:    2006:209947  BIOSIS
DOCUMENT NUMBER:     PREV200600211676
TITLE:               Critical role of the atypical lambda isoform, of PKC
                     (PKC-Lambda) in disruption of the cytoskeletal assembly in
                     monolayers of intestinal epithelium.
AUTHOR(S):           Banan, Ali; Zhang, Lijuan; Shaikh, Maliha; Fields, Jeremy
                     Z.; Farhadi, Ashkan; Keshavarzian, Ali
SOURCE:              Gastroenterology, (APR 2005) Vol. 128, No. 4, Suppl. 2, pp.
                     A537.
                     Meeting Info.: Annual Meeting of the American-
                     Gastroenterological-Association/Digestive-Disease-Week.
                     Chicago, IL, USA. May 14 -19, 2005. Amer Gastroenterol
                     Assoc.
                     CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE:       Conference; (Meeting)
                     Conference; Abstract; (Meeting Abstract)
LANGUAGE:            English
```

ENTRY DATE: Entered STN: 29 Mar 2006
Last Updated on STN: 29 Mar 2006

AB Oxidative injury to epithelial cells is a key factor in the pathogenesis of inflammatory bowel disease (IBD). Studying monolayers of **intestinal** cells, we reported that oxidants disrupt both the cytoskeleton and barrier function. Because the lambda (-lambda) isoform of PKC. an atypical DAG-independent isozyme, is abundant in parental Caco-2 cells and is translocated to the particulate fractions upon oxidant exposure, we hypothesized that PKC-lambda is critical to oxidant-induced disruption of cytoskeletal assembly and barrier function. Cells were transfected with an inducible plasmid to create novel clones stably overexpressing native PKC-lambda or with a dominant negative plasmid to stably inhibit the native PKC-lambda expression. Multiple clones were exposed to oxidant (H2O2) +/- modulators, Parental Caco-2 cells were treated similarly. We then monitored barrier function < **fluorometry** <<; cytoskeletal stability < confocal microscopy <<; PKC-lambda subcellular distribution < immunofluorescence, PAGE <<, PKC-lambda activity < immunoprecipitation, in vitro kinase assay <<, **tubulin** & actin assembly - polymerized (S2) and **monomeric** (S1) < SDS-PAGE fractionation <<. Results: < A << In parental cells, oxidants caused: translocation of PKC-lambda from cytosol to particulate (membrane + cytoskeletal) fractions, activation of native PKC-lambda; **tubulin**/actin instability (up arrow **monomeric** S1 & down arrow polymerized S2 pools), disruption of cytoskeletal architecture; and barrier dysfunction (hyperpermeability). & In transfected clones, over-expression of the atypical (74 kDa) PKC-lambda isoform (similar to 3.2 fold increase) led to oxidant-like disruptive effects, including cytoskeletal and barrier disruption. Over-expressed PKC-lambda was mostly found in cytoskeletal cell fractions (with a smaller cytosolic distribution), indicating its activation. Disruption induced by PKC-lambda overexpression was synergistic with that by oxidant. & Stable inactivation of endogenous PKC-lambda (similar to 99.9%) by a dominant negative protected against all measures of oxidant-induced disruption. We conclude that (1) oxidants disrupt epithelial integrity by disassembling the cytoskeleton, in part, through the activation of PKC-lambda isoform; (2) Activation of PKC-lambda by itself appears to be sufficient for disruption of cellular cytoskeleton and monolayer integrity. The unique ability to mediate oxidative injury and cytoskeletal depolymerization & instability are novel mechanisms not previously attributed to the atypical subfamily of PKC isoforms.

L46 ANSWER 2 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2004380272 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15283469
TITLE: Effects of dopamine HCl on structural parameters of bovine brain membranes.
AUTHOR: Bae Moon-Kyoung; Huh Min-Hoi; Lee Seung-Woo; Kang Hyun-Gu; Pyun Jae-Ho; Kwak Myeong-Hee; Jang Hye-Ock; Yun Il
CORPORATE SOURCE: College of Dentistry and Research Institute for Oral Biotechnology, Pusan National University, Pusan 602-739, Korea.
SOURCE: Archives of pharmacal research, (2004 Jun) Vol. 27, No. 6, pp. 653-61.
Journal code: 8000036. ISSN: 0253-6269.
PUB. COUNTRY: Korea (South)
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 1 Aug 2004

Last Updated on STN: 23 Apr 2005
Entered Medline: 22 Apr 2005

AB Fluorescence probes located in different membrane regions were used to evaluate the effect of dopamine.HCl on the structural parameters (transbilayer lateral mobility, annular lipid fluidity, protein distribution, and thickness of the lipid bilayer) of synaptosomal plasma membrane vesicles (SPMV), which were obtained from the bovine cerebral cortex. An experimental procedure was used based on selective quenching of 1,3-di(1-pyrenyl)propane (Py-3-Py) by trinitrophenyl groups, and radiationless energy transfer from the tryptophan of membrane proteins to Py-3-Py and energy transfer from Py-3-Py **monomers** to 1-anilinonaphthalene-8-sulfonic acid (**ANS**) was also utilized. Dopamine.HCl increased both the bulk lateral mobility and annular lipid fluidity, and it had a greater fluidizing effect on the inner monolayer than on the outer monolayer. Furthermore, the drug had a clustering effect on membrane proteins.

L46 ANSWER 3 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004020071 EMBASE
TITLE: Effect of Deamidation of Asparagine 146 on Functional and Structural Properties of Human Lens αB-Crystallin.
AUTHOR: Gupta R.; Srivastava O.P.
CORPORATE SOURCE: O.P. Srivastava, Department of Physiological Optics, Worrell Building, University of Alabama at Birmingham, 924 South 18th Street, Birmingham, AL 35294-4390, United States. srivasta@uab.edu
SOURCE: Investigative Ophthalmology and Visual Science, (2004) Vol. 45, No. 1, pp. 206-214. .
Refs: 46
ISSN: 0146-0404 CODEN: IOVSDA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004

AB PURPOSE. To elucidate the effect of deamidation on the structural and functional properties of human αB-crystallin. METHODS. Site-directed mutagenesis was used to generate three deamidated mutants of αB-crystallin: N78D, N146D, and N78D/N146D. The mutations were confirmed by DNA sequencing and matrix-assisted desorption ionization-time of flight (MALDI-TOF) mass spectrometry. Recombinant native αB-crystallin (wild type [WT]) and the three mutated αB species were expressed, and each species was purified to homogeneity by ion-exchange chromatography followed by hydrophobic interaction chromatography. The structural and functional properties compared with WT protein were investigated, respectively, by static light scattering (SLS), circular dichroism (CD), and fluorescence spectroscopy and by determining chaperone activity with the use of three substrates. RESULTS. Native WT and the N78D mutant showed relatively higher chaperone activity compared with the N146D and N78D/N146D mutants with all the substrates. Further, during binding experiments with 1-anilino-8-naphthalenesuaonate (**ANS**), the WT and N78D mutant showed relatively more solvent-exposed hydrophobic residues than the N146D and N78D/N146D mutants. On determining far-UV circular dichroism and tryptophan (Trp) fluorescence spectra, significant secondary and tertiary structural changes were observed in the N146D and N78D/N146D mutants compared with WT

and the N78D mutant. The static light scattering data showed a high order of **oligomerization** in all the three mutants. N146D and N78D/N146D formed the largest **oligomers** of 750 and 770 kDa, respectively, compared with WT (580 kDa). CONCLUSIONS. The results show that the deamidation of N(146) but not of N(78) have profound effects on the structural and functional properties of αB-crystallin.

L46 ANSWER 4 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:525982 BIOSIS
DOCUMENT NUMBER: PREV200300529267
TITLE: Fluorescence spectroscopy studies on micellization of poloxamer 407 solution.
AUTHOR(S): Lee, Kayoung; Shin, Sang-Chul; Oh, Injoon [Reprint Author]
CORPORATE SOURCE: College of Pharmacy, Chonnam National University, 300 Yongbong-Dong, Buk-Gu, Gwangju, 500-757, South Korea ijoh@chonnam.ac.kr
SOURCE: Archives of Pharmacal Research (Seoul), (August 2003) Vol. 26, No. 8, pp. 653-658. print.
CODEN: APHRDQ. ISSN: 0253-6269.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Nov 2003
Last Updated on STN: 12 Nov 2003

AB It has been reported that at low temperature region, poloxamers existed as a **monomer.** Upon warming, an equilibrium between unimers and micelles was established, and finally micelle aggregates were formed at higher temperature. In this study, the fluorescence spectroscopy was used to study the micelle formation of the poloxamer 407 in aqueous solution. The excitation and emission spectra of pyrene, a fluorescence probe, were measured as a function of the concentration of poloxamer 407 and temperature. A blue shift in the emission spectrum and a red shift in the excitation spectrum were observed as pyrene transferred from an aqueous to a hydrophobic micellar environment. From the I1/I3 and I339/I333 results, critical micelle concentration (cmc) and critical micelle temperature (cmt) were determined. Also, from the fluorescence spectra of the probe molecules such as 8-anilino-1-naphthalene sulfonic acid and 1-pyrenecarboxaldehyde, the blue shift of the lambdamax was observed. These results suggest a decrease in the polarity of the microenvironment around probe because of micelle formation. The poloxamer 407 above cmc strongly complexed with hydrophobic fluorescent probes and the binding constant of complex increased with increasing the hydrophobicity of the probe.

L46 ANSWER 5 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:582210 BIOSIS
DOCUMENT NUMBER: PREV200300572049
TITLE: ATYPICAL LAMBDA (LAMBDA) ISOFORM OF PKC (PKC-LAMBDA) IS A NOVEL MEDIATOR OF **INTESTINAL** BARRIER DISRUPTION & CYTOSKELETAL DISASSEMBLY AND ESSENTIAL IN OXIDATIVE CELLULAR INJURY.
AUTHOR(S): Banan, Ali [Reprint Author]; Fields, Jeremy Z. [Reprint Author]; Zhang, Lijuan [Reprint Author]; Shaikh, Maliha [Reprint Author]; Farhadi, Ashkan [Reprint Author]; Keshavarzian, Ali [Reprint Author]
CORPORATE SOURCE: Chicago, IL, USA
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. M1126. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association;

American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Gut barrier disruption and oxidant injury are key in the pathogenesis of inflammatory bowel disease (IBD). Using monolayers of **intestinal** (Caco-2) cells, we showed that oxidants disassemble & injure the microtubule (MT) cytoskeleton and disrupt barrier integrity (BI). Since the atypical PKC isoform apprxeq is present in oxidant exposed wild type (WT) **intestinal** cells, we sought to determine whether PKC-apprxeq is required for oxidant-induced cytoskeletal disassembly and monolayer barrier disruption. METHODS: WT cells were incubated with oxidants (e.g. H2O2) +- PKC modulators. We also created the first GI cells stably transfected with varying levels of plasmids to over-express PKC-apprxeq (inducible) or to inhibit activity of native PKC-apprxeq (dominant negative). These clones were then treated as above. We assessed BI (clearance by **fluorometry**); MT cytoskeletal integrity (laser confocal microscopy); PKC-apprxeq subcellular distribution (immunoblotting); PKC-apprxeq activity (in vitro kinase); polymerized (S2) & **monomeric** (S1) **tubulin** (50 kDa protein of microtubules, western blot), n=6/grp. RESULTS: {A} In WT cells, oxidant exposure caused: 1) translocation of PKC-apprxeq to particulate (membrane + cytoskeletal) fractions; 2) activation of PKC-apprxeq; 3) reduction in **tubulin** assembly (increased S1 & decreased S2); 4) disruption of cytoskeletal cytoarchitecture; & 5) loss of BI. {B} In transfected cells induction of PKC-apprxeq over-expression by itself (+3.2 fold), led to oxidant-like disruptive effects. All measures of disruption induced by PKC-apprxeq over-expression were potentiated by oxidants. Over-expressed PKC-apprxeq resided in particulate fractions, indicating its activation. {C} Stable inhibition of native PKC-apprxeq (-99%) with a dominant negative transfection substantially protected against oxidant injury as shown by enhanced stability of **tubulin** pools & cytoskeletal assembly, and monolayer BI to near normal levels. We show for the first time: 1) Oxidants induce loss of epithelial barrier integrity by disassembling the cytoskeleton, in part, through the activation of the PKC-apprxeq signaling; 2) Over-expression & activation of PKC-apprxeq is by itself a sufficient condition for disruption of these cytoskeleton and permeation pathways; 3) PKC-apprxeq is a endogenous destabilizer of cytoskeletal dynamics and key in cellular injury under oxidative (inflammatory like) conditions. Thus, PKC-apprxeq activation may play a key role in **intestinal** dysfunction in oxidant-induced diseases such as IBD..

L46 ANSWER 6 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:582211 BIOSIS
DOCUMENT NUMBER: PREV200300572050
TITLE: ZETA (zeta) ISOFORM OF PKC IS A UNIQUE MODULATOR OF NF-kappaB / I-kappaB-alpha IN THE **INTESTINAL** EPITHELIUM & CRITICAL TO MONOLAYER PROTECTION .
AUTHOR(S): Banan, Ali [Reprint Author]; Farhadi, Ashkan [Reprint Author]; Fields, Jeremy Z. [Reprint Author]; Shaikh, Maliha [Reprint Author]; Zhang, Lijuan [Reprint Author]; Keshavarzian, Ali [Reprint Author]
CORPORATE SOURCE: Chicago, IL, USA
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. T1044. e-file.

Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Gut barrier disruption & NF-kappaB activation are key in the pathogenesis of inflammatory GI illnesses. Using monolayers of **intestinal** (Caco-2) cells, we observed that oxidants activate NF-kappaB by degrading its modulator I-kappaBalpha & lead to disruption of microtubule (MT) cytoskeleton & barrier integrity (BI). EGF prevents these processes, but the mechanisms are unclear. Since the atypical zeta isoform of PKC is key in cell maintenance, we investigated whether PKC-zeta is essential in EGF protection against oxidant induced I-kappaBalpha degradation & NF-kappaB activation and consequent cytoskeletal & BI disruption. METHODS: We used the first GI clones created by stable transfection to either overexpress the PKC-zeta or to inhibit its expression. Clones were then preincubated with EGF or PKC activators +- oxidant (H2O2). Wild type (WT) cells were treated similarly. We monitored monolayer BI (clearance by **fluorometry**), MT cytoskeleton (laser confocal microscopy), PKC-zeta subcellular distribution (immunoblotting), PKC-zeta activity (in vitro kinase), I-kappaBalpha levels (immunoblotting), NF-kappaB nuclear translocation & activity (immunoblotting, ELISA); polymerized (S2) & **monomeric** (S1) **tubulin** (50 kDa structural protein of MT, western blot), n=6/grp. RESULTS: {A} Relative to WT cells exposed to oxidant alone, either the monolayers of transfected cells stably overexpressing the PKC-zeta (+2.9 fold) or the WT cells pretreated with EGF were protected against injury as indicated by enhanced PKC-zeta activation, I-kappaBalpha stabilization; NF-kappaB inactivation (p50 and p65 subunits); **tubulin** assembly (increased S2, decreased S1), MT cytoarchitectural integrity; & monolayer BI to near normal. {B} All measures of protection induced by PKC-zeta were potentiated by EGF. Most of the overexpressed PKC-zeta resided in membrane & cytoskeletal fractions (with less than 10% in cytosolic fractions), indicating constitutive activation of zeta. {C} Antisense transfection to stably inhibit the native PKC-zeta expression & activity (-99%) prevented all measures of EGF protection, increased I-kappaBalpha degradation, NF-kappaB activation, & monolayer disruption. We show for the first time that: 1) Activation of PKC-zeta is necessary for cellular protection against stress of NF-kappaB activation; 2) PKC-zeta is a unique intracellular modulator of I-kappaBalpha in **intestinal** cells; 3) We have identified a novel biologic mechanism, protection of cytoskeletal & barrier integrity through the stabilization of I-kappaBalpha and inactivation NF-kappaB, among the PKC family of isoforms in cells..

L46 ANSWER 7 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:582212 BIOSIS
DOCUMENT NUMBER: PREV200300572051
TITLE: EVIDENCE THAT NF-kappaB ACTIVATION IS CRITICAL TO OXIDANT DISRUPTION OF CYTOSKELETON & BARRIER INTEGRITY (BI) AND THAT ITS INACTIVATION IS KEY TO EGF PROTECTION OF MONOLAYERS OF **INTESTINAL** EPITHELIA.
AUTHOR(S): Banan, Ali [Reprint Author]; Farhadi, Ashkan [Reprint Author]; Fields, Jeremy [Reprint Author]; Zhang, Lijuan [Reprint Author]; Shaikh, Maliha [Reprint Author];

Keshavarzian, Ali [Reprint Author]
CORPORATE. SOURCE: Chicago, IL, USA
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 858. e-file. Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Gut barrier disruption and oxidant injury are key in the pathogenesis of inflammatory bowel disease (IBD). Using monolayers of **intestinal** (Caco-2) cells, we showed that oxidants disassemble the microtubule (MT) cytoskeleton & disrupt BI and that growth factor (EGF) protects against these injuries. Since proinflammatory conditions induce NF-kappaB by degrading I-kappaBalpha, we hypothesized that oxidant induces disruption of monolayers through degradation of I-kappaBalpha & subsequent activation of NF-kappaB and that EGF mediates protection by suppressing these injurious processes. METHODS: Parental cells were pretreated with EGF or NF-kappaB modulators +- oxidant (H2O2). Cells were also stably transfected with varying levels of a dominant mutant for I-kappaBalpha to inhibit its degradation & then exposed to oxidant +- modulators. We monitored BI (**fluorometry**); MT cytoskeleton (laser confocal microscopy); I-kappaBalpha cytosolic levels (immunoblotting); NF-kappaB nuclear translocation & activity (immunoblotting, ELISA), polymerized (S2) & **monomeric** (S1) **tubulin** (50 kDa protein of MT, western blot), n=6/grp. RESULTS: {A} Oxidants caused degradation of I-kappaBalpha, translocation of NF-kappaB to nucleus, activation of NF-kappaB p50 & p65 subunits, instability of **tubulin** assembly (S1 & S2 pools), disruption of MT cytoarchitecture, and loss of BI. Any of I-kappaBalpha stabilizers or NF-kappaB inhibitors (e.g., MG-132, lactacystin) substantially suppressed oxidants effects. {B} EGF stabilized I-kappaBalpha and prevented both translocation & activation of NF-kappaB while protecting the parental monolayers against oxidants. {C} In mutant transfected cells stabilization of I-kappaBalpha by itself led to EGF-like protective effects. All measures of protection induced by mutant I-kappaBalpha stabilization were potentiated by low doses of EGF. We show for the first time that: 1) Oxidants induce disruption of the cytoskeleton and **intestinal** barrier integrity largely through NF-kappaB activation; 2) I-kappaBalpha stabilization is by itself protective, mimicking EGF. 3) EGF appears to protect cell monolayers through I-kappaBalpha stabilization and NF-kappaB inactivation. 4) We have discovered new functions for the NF-kappaB, alterations to cytoskeletal assembly & cytoarchitecture and epithelial barrier integrity. Suppressing NF-kappaB activation (by EGF mimetics) is a potentially useful strategy for treating inflammatory disorders (e.g., IBD) that are associated with oxidant injury..

L46 ANSWER 8 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2002293937 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12033951
TITLE: Complementation of buried lysine and surface polar residues in a designed **heterodimeric** coiled coil.
AUTHOR: Campbell Kathleen M; Lumb Kevin J
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Colorado

State University, Fort Collins, Colorado 80523-1870, USA.
CONTRACT NUMBER: RR11847 (NCRR)
RR11981 (NCRR)
SOURCE: Biochemistry, (2002 Jun 4) Vol. 41, No. 22, pp. 7169-75.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 30 May 2002
Last Updated on STN: 7 Jul 2002
Entered Medline: 5 Jul 2002

AB The coiled coil is an attractive target for protein design. The helices of coiled coils are characterized by a heptad repeat of residues denoted a to g. Residues at positions a and d form the interhelical interface and are usually hydrophobic. An established strategy to confer structural uniqueness to two-stranded coiled coils is the use of buried polar Asn residues at position a, which imparts **dimerization** and conformational specificity at the expense of stability. Here we show that polar interactions involving buried position-a Lys residues that can interact favorably only with surface e' or g' Glu residues also impart structural uniqueness to a designed **heterodimeric** coiled coil with the nativelike properties of sigmoidal thermal and urea-induced unfolding transitions, slow hydrogen exchange and lack of **ANS** binding. The position-a Lys residues do not, however, confer a single preference for helix orientation, likely reflecting the ability of Lys at position a to from favorable interactions with g' or e' Glu residues in the parallel and antiparallel orientations, respectively. The Lys-Glu polar interaction is less destabilizing than the Asn-Asn a-->a' interaction, presumably reflecting a higher desolvation penalty associated with the completely buried polar position-a groups. Our results extend the range of approaches for two-stranded coiled-coil design and illustrate the role of complementing polar groups associated with buried and surface positions of proteins in protein folding and design.

L46 ANSWER 9 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002110377 EMBASE
TITLE: Lead ion effect on creatine kinase: Equilibrium and kinetic studies of inactivation and conformational changes.
AUTHOR: Zhou H.-W.; Park Y.-D.; Zhou H.-M.
CORPORATE SOURCE: H.-M. Zhou, Department of Biological Science, Tsinghua University, Beijing 100084, China. zhm-dbs@mail.tsinghua.edu.cn
SOURCE: International Journal of Biochemistry and Cell Biology, (2002) Vol. 34, No. 5, pp. 564-571. .
Refs: 35
ISSN: 1357-2725 CODEN: IJBBFU
PUBLISHER IDENT.: S 1357-2725(01)00145-5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Apr 2002
Last Updated on STN: 4 Apr 2002

AB The effects of lead ions on creatine kinase (CK) were studied by measuring activity changes, intrinsic fluorescence spectra and 8-anilo-1-naphthalenesulfonate (**ANS**)-binding fluorescence along with

size-exclusion chromatography (SEC). Below 5mM Pb(2+) concentration, there was nearly no change of the enzyme activity and a slight change of the **ANS**-binding fluorescence. The CK activity decreased significantly from 10 to 25mM Pb(2+) concentrations. No residual activity was observed above 25mM Pb(2+). The kinetic time courses of inactivity and unfolding were all mono-phase courses with the inactivation rate constants being greater than the unfolding rate constants for the same Pb(2+) concentration. The changes in fluorescence maximum and fluorescence intensity were relatively slow for 40-80mM Pb(2+) as well as in the initial stage for less than 5mM Pb(2+), showing that two transition states exist for Pb(2+) induced equilibrium-unfolding curves. The intrinsic fluorescence spectra and **ANS**-binding fluorescence measurements showed that even for high Pb(2+) concentrations, CK did not fully unfold. Additionally, the SEC results showed that the enzyme molecule still existed in an inactive **dimeric** state at 20 and 40mM Pb(2+) solutions. All the results indicated the presence of at least one stable unfolding equilibrium intermediate of CK during Pb(2+) unfolding. .COPYRGT. 2002 Elsevier Science Ltd. All rights reserved.

L46 ANSWER 10 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003160003 EMBASE
TITLE: Trichomonas vaginalis: Microtubule cytoskeleton distribution using fluorescent taxoid.
AUTHOR: Lecke S.B.; Tasca T.; Souto A.A.; De Carli G.A.
CORPORATE SOURCE: G.A. De Carli, Lab. de Parasitologia Clinica, Faculdade de Farmacia, Pont. Univ. Catol. Rio Grande do Sul, Porto Alegre, RS, Brazil. gdecarli@portoweb.com.br
SOURCE: Experimental Parasitology, (1 Oct 2002) Vol. 102, No. 2, pp. 113-116. .
Refs: 25
ISSN: 0014-4894 CODEN: EXPAAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 1 May 2003

AB Trichomonas vaginalis is a flagellated parasitic protist of the human urogenital tract. The parasite has a poorly known cytoskeleton formed by an axostyle and a pelta, which are formed by stable structures such as microtubules, essential for the maintenance of cell shape and organization. FLUTAX-2 is an active fluorescent derivative of Taxol, binds to αβ- **tubulin dimer** polymerized. In this paper we present the analysis of microtubule distribution in living trophozoites of T. vaginalis using FLUTAX-2. .COPYRGT. 2003 Published by Elsevier Science (USA).

L46 ANSWER 11 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:167569 BIOSIS
DOCUMENT NUMBER: PREV200200167569
TITLE: Identification of specific proteins in different lymphocyte populations by proteomic tools.
AUTHOR(S): Vuadens, Francoise; Gasparini, Danielle; Deon, Catherine; Sanchez, Jean-Charles; Hochstrasser, Denis F.; Schneider, Philippe; Tissot, Jean-Daniel [Reprint author]
CORPORATE SOURCE: Service Regional Vaudois de Transfusion Sanguine, Rue du Bugnon 27, CH-1005, Lausanne, Switzerland

jean-daniel.tissot@chuv.hospvd.ch
SOURCE: Proteomics, (January, 2002) Vol. 2, No. 1, pp. 105-111. print.
ISSN: 1615-9853.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002

AB The solubilized proteins of purified CD19+ (B), CD8+ (T) as well as CD4+ (T) lymphocytes were separated by high resolution two-dimensional polyacrylamide gel electrophoresis, and the gels were analyzed using Melanie 3.0. Nine gels were studied, three for each lymphocyte population. After image analysis, 1411+-73 spots (mean+SD) were detected. The protein pattern of B lymphocytes segregated from the one of T lymphocytes by ascendant heuristic clustering analysis. In addition, computer analysis separated CD8+ from CD4+ lymphocytes. When a search was performed in order to detect subsets of specific spots (presence vs. absence), a group of three spots, detected in the area of the protein maps corresponding to isoelectric point (p/) of 5.2 to 5.4 and molecular weight (Mr) of 50 to 51 kDa, were found in both CD8+ and CD4+ cells, but not in CD19+ cells. Mass spectrometry analysis revealed that these spots were associated with **several** proteins such as vimentin, **tubulin**, desmin and cytokeratin. Two spots, located in the area of the gel corresponding to p/ of about 5.0 and a Mr of 30 kDa, appeared as CD8+ cell associated. Mass spectrometry analysis showed that the two spots were related to the same non-identified protein. Moreover internal peptides sequences matched with two human expressed sequence tags: gil9759776, gil12798420. No spots were found as only B cell associated.

L46 ANSWER 12 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:512068 BIOSIS
DOCUMENT NUMBER: PREV200100512068
TITLE: Clusterin, a binding protein with a molten globule-like region.
AUTHOR(S): Bailey, Robert W.; Dunker, A. Keith; Brown, Celeste J.; Garner, Ethan C.; Griswold, Michael D. [Reprint author]
CORPORATE SOURCE: School of Molecular Biosciences, Washington State University, Pullman, WA, 99164-4660, USA
griswold@mail.wsu.edu
SOURCE: Biochemistry, (October 2, 2001) Vol. 40, No. 39, pp. 11828-11840. print.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002

AB Clusterin is a **heterodimeric** glycoprotein found in many tissues of the body and is the most abundant protein secreted by cultured rat Sertoli cells. The function of clusterin is unknown, but it has been associated with cellular injury, lipid transport, apoptosis, and it may be involved in the clearance of cellular debris caused by cell injury or death. Consistent with this last idea, clusterin has been shown to bind to a variety of molecules with high affinity including lipids, peptides, and proteins and the hydrophobic probe 1-anilino-8-naphthalenesulfonate (**ANS**). Given this variety of ligands, clusterin must have specific structural features that provide the protein with its promiscuous binding activity. Using sequence analyses, we show that clusterin likely contains three long regions of natively disordered or molten globule-like structures containing putative amphipathic alpha-helices. These

disordered regions were highly sensitive to trypsin digestion, indicating a flexible nature. The effects of denaturation on the fluorescence of the clusterin-**ANS** complex were compared between proteins with structured binding pockets and molten globular forms of proteins. Clusterin bound **ANS** in a manner that was very similar to that of molten globular proteins. Furthermore, we found that, when bound to **ANS**, at least one cleavage site within the protease-sensitive disordered regions of clusterin was protected from trypsin digestion. In addition, we show that clusterin can function as a biological detergent that can solubilize bacteriorhodopsin. We propose that natively disordered regions with amphipathic helices form a dynamic, molten globule-like binding site and provide clusterin the ability to bind to a variety of molecules.

L46 ANSWER 13 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:140750 BIOSIS
DOCUMENT NUMBER: PREV199900140750
TITLE: Folding and assembly of an antibody Fv fragment, a **heterodimer** stablized by antigen.
AUTHOR(S): Jaeger, Marcus; Plueckthun, Andreas [Reprint author]
CORPORATE SOURCE: Biochemisches Institut, Univ. Zurich, Winterthurerstr. 190, CH-8057 Zurich, Switzerland
SOURCE: Journal of Molecular Biology, (Feb. 5, 1999) Vol. 285, No. 5, pp. 2005-2019. print.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 1999
Last Updated on STN: 31 Mar 1999

AB The folding and assembly of the Fv fragment of the phosphorylcholine binding antibody McPC603, a non-covalent **heterodimer** of the variable domains VH and VL, was investigated. Since both domains, each engineered for stability and folding efficiency, could now be obtained in native and soluble form by themselves, fluorescence spectra of VH and VL in unfolded, folded and associated states can be reported. VH and VL only associate when they are native, and the stability of the **heterodimer** is strongly increased in the presence of antigen. VH rapidly folds into an hyperfluorescent intermediate, and the native state is reached in two parallel, proline-independent reactions. VL displays two fast refolding reactions, which are followed by two slower phases, limited by proline cis/trans-isomerization. The rate-limiting step for both the Fv and the scFv (single-chain Fv) fragment is the formation of the native VH-VL interface, which depends on ProL95 being in cis. The folding of the Fv fragment is fast after short-term denaturation or in the presence of proline cis/trans-isomerase catalysis, but the scFv fragment falls into a kinetic trap, observed by the persistence of the slow phases under all conditions. Furthermore, the scFv fragment, but not the Fv fragment, gives rise to premature interface formation, indicated by the fluorescence spectra and a much higher transient binding of 8-anilino-1-naphthalene sulfonate. The analysis of the folding pathway of the domains VH and VL in isolation and in non-covalent and covalent assemblies should provide helpful insights into the folding of multimeric proteins in general, and for the further engineering of stable and well-folding antibody fragments in particular.

L46 ANSWER 14 OF 33 MEDLINE on STN

ACCESSION NUMBER: 1998334608 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9668057
TITLE: Binding of Ca2+ and Zn2+ to human nuclear S100A2 and mutant

proteins.
AUTHOR: Franz C; Durussel I; Cox J A; Schafer B W; Heizmann C W
CORPORATE SOURCE: Department of Pediatrics, Division of Clinical Chemistry and Biochemistry, University of Zurich, CH-8032 Zurich, Switzerland.
SOURCE: The Journal of biological chemistry, (1998 Jul 24) Vol. 273, No. 30, pp. 18826-34.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 28 Aug 1998
Last Updated on STN: 28 Aug 1998
Entered Medline: 20 Aug 1998

AB The Ca2+-binding protein S100A2 is an unusual member of the S100 family, characterized by its nuclear localization and down-regulated expression in tumorigenic cells. In this study, we investigated the properties of human recombinant S100A2 (wtS100A2) and of two mutants in which the amino-terminal Ca2+-binding site I (N mutant) and in addition the carboxyl-terminal site II (NC mutant) were replaced by the canonical loop (EF-site) of alpha-parvalbumin. Size exclusion chromatography and circular dichroism showed that, irrespective of the state of cation binding, wtS100A2 and mutants are **dimers** and rich in alpha-helical structure. Flow dialysis revealed that wtS100A2 binds four Ca2+ atoms per **dimer** with pronounced positive cooperativity. Both mutants also bind four Ca2+ atoms but with a higher affinity than wtS100A2 and with negative cooperativity. The binding of the first two Ca2+ ions to the N mutant occurred with 100-fold higher affinity than in wtS100A2 and a 2-fold increase for the last two Ca2+ ions. A further 2-3-fold increase of affinity was observed for respective binding steps of the NC mutant. The Hummel-Dryer method demonstrated that the wild type and mutants bind four Zn2+ atoms per **dimer** with similar affinity. Fluorescence and difference spectrophotometry showed that the binding of Ca2+ and Zn2+ induces considerable conformational changes, mostly attributable to changes in the microenvironment of Tyr76 located in site II. Fluorescence enhancement of 4,4'-dianilino-1, 1'-binaphthyl-5,5'-disulfonic acid clearly indicated that Ca2+ and Zn2+ binding induce a hydrophobic patch at the surface of wtS100A2, which, as in calmodulin, may be instrumental for the regulatory role of S100A2 in the nucleus.

L46 ANSWER 15 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:360595 BIOSIS
DOCUMENT NUMBER: PREV199800360595
TITLE: **Dimeric** tyrosyl-tRNA synthetase from Bacillus stearothermophilus unfolds through a **monomeric** intermediate: A quantitative analysis under equilibrium conditions.
AUTHOR(S): Park, Young Chul; Bedouelle, Hugues [Reprint author]
CORPORATE SOURCE: Groupe d'Ingenierie des Proteines, Unite de Biochimie Cellulaire, Institut Pasteur, 28 rue du Docteur Roux, 75724 Paris Cedex 15, France
SOURCE: Journal of Biological Chemistry, (July 17, 1998) Vol. 273, No. 29, pp. 18052-18059. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 27 Aug 1998
Last Updated on STN: 27 Aug 1998

AB Tyrosyl-tRNA synthetase from Bacillus stearothermophilus comprises an N-terminal domain (residues 1-319), which is **dimeric** and forms tyrosyladenylate, and a C-terminal domain (residues 320-419), which binds the anticodon arm of tRNATyr. The N-terminal domain has the characteristic fold of the class I aminoacyl-tRNA synthetases. The unfolding of the N-terminal domain by urea at 25degree C under equilibrium conditions was monitored by its intensities of light emission at 330 and 350 nm, the ratio of these intensities, its ellipticity at 229 nm, and its partition coefficient, in **spectrofluorometry**, circular dichroism, and size-exclusion chromatography experiments, respectively. These experiments showed the existence of an equilibrium between the native **dimeric** state of the N-terminal domain, a **monomeric** intermediate state, and the unfolded state. The intermediate was compact and had secondary structure, and its tryptophan residues were partially buried. These properties of the intermediate and its inability to bind 1-anilino-8-naphthalenesulfonate showed that it was not in a molten globular state. The variation of free energy DELTAG(H2O) and its coefficient m of dependence on the concentration of urea were, respectively, 13.8 +- 0.2 kcalcntdotmol-1 and 0.9 +- 0.1 kcalcntdotmol-1cntdotM-1 for the dissociation of the native **dimer** and 13.9 +- 0.6 kcalcntdotmol-1 and 2.5 +- 0.1 kcalcntdotmol-1cntdotM-1 for the unfolding of the **monomeric** intermediate.

L46 ANSWER 16 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:491188 BIOSIS
DOCUMENT NUMBER: PREV199800491188
TITLE: Peptide models of local and long-range interactions in the molten globule state of human alpha-lactalbumin.
AUTHOR(S): Demarest, Stephen J.; Fairman, Robert; Raleigh, Daniel P. [Reprint author]
CORPORATE SOURCE: Dep. Chem., State Univ. New York Stony Brook, Stony Brook, NY 11794-3400, USA
SOURCE: Journal of Molecular Biology, (Oct. 16, 1998) Vol. 283, No. 1, pp. 279-291. print.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Nov 1998
Last Updated on STN: 18 Nov 1998

AB alpha-Lactalbumin, a small calcium-binding protein, forms an equilibrium molten globule state under a variety of conditions. A set of four peptides designed to probe the role of local interactions and the role of potential long-range interactions in stabilizing the molten globule of alpha-lactalbumin has been prepared. The first peptide consists of residues 20 through 36 of human alpha-lactalbumin and includes the entire B-helix. This peptide is unstructured in solution as judged by CD. The second peptide is derived from residues 101 through 120 and contains both the D and 310 helices. When this peptide is crosslinked via the native 28 to 111 disulfide to the B-helix peptide, a dramatic increase in helicity is observed. The crosslinked peptide is **monomeric**, as judged by analytical ultracentrifugation. The peptide binds 1-anilinonaphthalene-8-sulphonate (**ANS**) and the fluorescence emission maximum of the construct is consistent with partial solvent exposure of the tryptophan residues. The peptide corresponding to residues 101 to 120 adopts significant non-random structure in aqueous solution at low pH. Two hydrophobic clusters, one involving residues 101 through 104 and the other residues 115 through 119 have been identified and characterized by NMR.

The hydrophobic cluster formed by residues 101 through 104 is still present in a smaller peptide containing only residues 101 to 111 of alpha-lactalbumin. The cluster also persists in 6 M urea. A non-native, pH-dependent interaction between the Y103 and H107 side-chains that was previously identified in the acid-denatured molten globule state was examined. This interaction was found to be more prevalent at low pH and may therefore be an example of a local interaction that stabilizes preferentially the acid-induced molten globule state.

L46 ANSWER 17 OF 33 EMBASE

ACCESSION NUMBER: 97120011 EMBASE
DOCUMENT NUMBER: 1997120011
TITLE: Characterization of the equilibrium intermediates in acid denaturation of human stefin B.
AUTHOR: Zerovnik E.; Jerala R.; Kroon-Zitko L.; Turk V.; Lohner K.
CORPORATE SOURCE: E. Zerovnik, Dept. Biochemistry/Molecular Biology, J. Stefan Institute, P.O.B, 100, SLO-1001 Ljubljana, Slovenia
SOURCE: European Journal of Biochemistry, (1997) Vol. 245, No. 2, pp. 364-372. .
Refs: 52
ISSN: 0014-2956 CODEN: EJBCAI
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 May 1997
Last Updated on STN: 20 May 1997

AB Acid-induced denaturation of recombinant human stefin B was followed using circular dichroism (CD) and fluorimetry. By comparing different spectroscopic probes, a number of equilibrium intermediates were detected. In pH denaturation at very low salt concentration (0.3 M NaCl) four states can be distinguished: N - I(N) - I1 - U, where N is the native state, I(N) is a native-like intermediate, I1 is an acid intermediate state with properties of a molten globule and U is the unfolded state. State I, exhibits no near-ultraviolet CD but has some residual far-ultraviolet CD. It differs from U in its ability to increase fluorescence of 1-anilino-naphthalene 8-sulfonate (**ANS**). In 0.42 M salt, the pH denaturation is three-state between the **dimeric** native state N2 and intermediates I(N2) and I2, which are also **dimeric** according to size-exclusion chromatography. The acid intermediate I2 is more structured than I1: it binds **ANS** to a lower extent an I1, its Tyr residues are protected from the solvent, it shows; some near-ultraviolet CD and its far-ultraviolet CD is even more intense than that for the native state. 1H-NMR-spectra confirmed the overall structural features of the acid intermediates. To obtain the enthalpies of unfolding, microcalori metric measurements were performed under conditions where the acid intermediates are maximally populated (18°C): state I(N) from pH 5.0 to 4.6, 0.03 M salt; state I2 below pH 3.8, 0.42 M salt; and state I1 in equilibrium with I(N) at pH 4.05, 0.03 M salt. Enthalpies of unfolding for states I(N) and I2 were comparable to those of the native state. The enthalpy of unfolding for state I1 could not be determined.

L46 ANSWER 18 OF 33 EMBASE

ACCESSION NUMBER: 96321721 EMBASE
DOCUMENT NUMBER: 1996321721
TITLE: **Tubulin** conformation and dynamics: A red edge excitation shift study.

AUTHOR: Guha S.; Rawat S.S.; Chattopadhyay A.; Bhattacharyya B.
CORPORATE SOURCE: Department of Biochemistry, Bose Institute, Centenary Building, P-1/12 C. I. T. Scheme VII M,Calcuttta 700 054, India
SOURCE: Biochemistry, (1996) Vol. 35, No. 41, pp. 13426-13433. .
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 1996
Last Updated on STN: 19 Nov 1996

AB The fluorescence emission maximum of a polar fluorophore in viscous medium often shows a dependence on excitation wavelength, a phenomenon which is named red edge excitation shift (REES). We have found that the fluorescence spectra of the **tubulin** tryptophans exhibit a REES of about 7 nm. Also, their steady state fluorescence polarization and mean lifetimes show a dependence on both excitation and emission wavelengths. These results indicate that the average tryptophan environment in **tubulin** is motionally restricted. Although the tryptophan(s) responsible for the observed REES effect could not be localized, it could be concluded from energy transfer experiments with the **tubulin**-colchicine complex that the tryptophan(s) participating in energy transfer with bound colchicine probably does not contribute to the REES. A REES of 7 nm was also observed in the case of colchicine complexed with **tubulin.** However, such a REES was not seen in similar studies with the B-ring analogs of colchicine, viz. 2-methoxy-5-(2',3',4'-trimethoxyphenyl)tropone (called AC because it lacks the B ring of colchicine) and deacetamidocolchicine (which lacks the acetamido substituent at the C-7 position of the B ring). There may be two possible reasons to explain these data. (1) Structural differences between colchicine and its analogs may give rise to differences in their excited state dipole moments which will directly affect the extent of REES, and (2) The B-ring substituent, hanging outside the colchicine binding site on the β-subunit of the **tubulin dimer**, probably makes **contact** with the α-subunit of **tubulin** and imparts a rigidity to that region of the protein, which facililates the REES.

L46 ANSWER 19 OF 33 MEDLINE on STN
ACCESSION NUMBER: 96330425 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8755027
TITLE: [A comparative study of the action of 1-methyl-1-nitrosourea and 1,3-dimethyl-1-nitrosourea on tumor cell DNA in vitro and in vivo by the alkaline elution method]. Sravnitel'noe izuchenie deistviia 1-metil-1-nitrozomocheviny i 1,3-dimetil-1-nitrozomocheviny na DNK opukholevykh kletok in vitro i in vivo metodom shchelochnoi eliutsii.
AUTHOR: Bliukhterova N V; Smotriaeva M A; Krugliakova K E
SOURCE: Izvestiia Akademii nauk. Seriia biologicheskaia / Rossiiskaia akademiia nauk, (1996 May-Jun) No. 3, pp. 276-81.
Journal code: 9300152. ISSN: 1026-3470.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610

ENTRY DATE: Entered STN: 15 Oct 1996
Last Updated on STN: 30 Oct 2002
Entered Medline: 2 Oct 1996

AB DNA damage of the tumor cells was studied by the method of alkali elution from filters after introduction of 1-methyl-1-nitrosourea (MNU) and 1,3-dimethyl-1-nitrosourea (DMNU) to mice with Ehrlich ascites carcinoma or after treatment of the cultivated cells with these drugs. DNA was essay fluorometrically using **DAPI**. The degree of DNA damage was characterized by the constant of the alkali elution rate (Kae), which was estimated according to the anamorphism of the kinetic curves of elution. It was shown that in the case of MNU application the tumor cell DNA was damaged to a greater extent than in the case of DMNU application. Kae increased with the concentration of drugs. A correlation was established between the antitumor activity of the drug (kappa), K(ae), and the number of chromosome defects per cell (gaps, deletions, microfragments, ring chromosomes, and translocations). This suggests that kappa is due both to DNA damage and chromosome defects.

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ACCESSION NUMBER: 94244097 EMBASE
DOCUMENT NUMBER: 1994244097
TITLE: Morphological and physicochemical changes in the myosin molecules induced by hydrostatic pressure.
AUTHOR: Yamamoto K.; Yoshida Y.; Morita J.; Yasui T.
CORPORATE SOURCE: Department of Food Science, Rakuno Gakuen University,Ebetsu, Hokkaido 069, Japan
SOURCE: Journal of Biochemistry, (1994) Vol. 116, No. 1, pp. 215-220. .
ISSN: 0021-924X CODEN: JOBIAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Aug 1994
Last Updated on STN: 17 Aug 1994

AB Hydrostatic pressure-induced morphological and physicochemical changes in **monomeric** myosin were investigated. The turbidity of a myosin solution increased after release of pressure, indicating aggregation of the molecules. Some molecules were single headed after exposure to 100-200 MPa, in contrast with an intact molecule having two heads. Small-sized **oligomeric** species, composed of several molecules, appeared after pressurization at 200 MPa. The **oligomers** were formed only through head-to-head association. Neither head-to-tail nor tail-to-tail interaction was observed. With increasing pressure to 300 MPa, **monomeric** myosin remarkably decreased, and most molecules formed **oligomers**, in which the myosin heads were tightly associated, forming a clump, the tails of the myosin molecules extending radially from the clump. Such an **oligomer** was shaped like a daisy wheel and its morphology was quite similar to that formed on heating reported previously. The aggregation of myosin molecules upon pressurization was concomitant with an increase in hydrophobicity, which was measured spectrofluorometrically with 8-anilino-1-naphthalene sulfonate, a probe for apolar binding sites. Although the turbidity increased continuously with increasing pressure, the hydrophobicity remained at; a constant level above 200 MPa at pH 6.0 and above 300 MPa at pH 7.0. The loss of myosin ATPase activity was accompanied by aggregation of the molecules. These results indicate that hydrophobic groups in the heads of myosin are exposed to the surface of the molecule on

pressurization, so that hydrophobic interaction among the heads occurs, yielding aggregates. Beside the hydrophobic interaction, the contribution of other interaction(s) is also suggested.

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ACCESSION NUMBER: 92201331 EMBASE
DOCUMENT NUMBER: 1992201331
TITLE: Conformational states of ribulosebisphosphate carboxylase and their interaction with chaperonin 60.
AUTHOR: Van der Vies S.M.; Viitanen P.V.; Gatenby A.A.; Lorimer G.H.; Jaenicke R.
CORPORATE SOURCE: Molecular Biology Division, Central Research/Development Dept., Dupont Company Experimental Station,Wilmington, DE 19880-0402, United States
SOURCE: Biochemistry, (1992) Vol. 31, No. 14, pp. 3635-3644. . ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 1992
Last Updated on STN: 2 Aug 1992

AB Conformational states of ribulosebisphosphate carboxylase (Rubisco) from Rhodospirillum rubrum were examined by far-UV circular dichroism (CD), tryptophan fluorescence, and 1-anilino-naphthalenesulfonate (**ANS**) binding. At pH 2 and low ionic strength (I = 0.01), Rubisco adopts an unfolded, **monomeric** conformation (UA1 state) as judged by far-UV CD and tryptophan fluorescence. As with other acid-unfolded proteins [Goto, Y., Calciano, L. J., and Fink, A. L. (1990) Proc. Natl. Acad. Sci. U.S.A. 87, 573-577], an intermediate conformation (A1 state) is observed at pH 2 and high ionic strength. The A1 state has an α-helical content equivalent to 64% of that present in the native **dimer** (N2 state). However, fluorescence measurements indicate that the tertiary structure of the A1 state is largely disordered. A site- directed mutant, K168E, which exists as a stable **monomer** [Mural, R. J., Soper, T. S., Larimer, F. W., and Hartman, F. C. (1990) J. Biol. Chemical 265, 6501-6505] was used to characterize the 'native' **monomer** (N1 state). The far-UV CD spectra of the N1 and N2 states are almost identical, indicating a similar secondary structure content. However, the tertiary structure of the N1 state is less ordered than that of the N2 state. Nevertheless, when appropriately complemented in vitro, K168E forms an active **heterodimer.** Upon neutralization of acid-denatured Rubisco or dilution of guanidine hydrochloride-denatured Rubisco, unstable folding intermediates (I1 state) are rapidly formed. At concentrations at or below the 'critical aggregation concentration' (CAC), the I1 state reverts spontaneously but slowly to the native states with high yield (>65%). The CAC is temperature-dependent. At concentrations above the CAC, the I1 and the A1 states undergo irreversible aggregation. The commitment to aggregation is rapid [cf. Goldberg, M. E., Rudolph, R., and Jaenicke, R. (1991) Biochemistry 30, 2790-2797] and proceeds until the concentration of folding intermediate(s) has fallen to the CAC. In the presence of a molar excess of chaperonin 60 **oligomers**, the I1 state forms a stable binary complex. No stable binary complex between chaperonin 60 and the N1 state could be detected. Formation of the chaperonin 60-I1 binary complex arrests the spontaneous folding process. The I1 state becomes resistant to interaction with chaperonin 60 with kinetics indistinguishable from those associated with the appearance of the native states. In vitro complementation analysis indicated that the

product of the chaperonin- facilitated process is **monomeric.** Spectral analyses of the I1 state, performed at concentrations below the CAC and before significant reversal to the native states had occurred, show that it possesses a similar secondary structure content to the A1 state but, like the N1 state, lacks the organized tertiary structure typical of the N2 state. The I1 state is considerably more sensitive to proteolysis than the N2 state, whether free in solution or bound to chaperonin 60.

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ACCESSION NUMBER: 92031554 EMBASE
DOCUMENT NUMBER: 1992031554
TITLE: Interactions of colchicine with **tubulin.**
AUTHOR: Hastie S.B.
CORPORATE SOURCE: Department of Chemistry, State University of New York, University Center, P.O. Box 6000, Binghamton, NY 13902-6000, United States
SOURCE: Pharmacology and Therapeutics, (1991) Vol. 51, No. 3, pp. 377-401. .
ISSN: 0163-7258 CODEN: PHTHDT
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 1992
Last Updated on STN: 20 Mar 1992

AB Colchicine exerts its biological effects through binding to the soluble **tubulin heterodimer**, the major component of the microtubule. The colchicine-binding abilities of **tubulins** from a variety of sources are summarized, and the mechanism of colchicine binding to brain **tubulin** is explored in depth. The relationship between colchicinoid structure and **tubulin** binding activity provides insight into the structural features of colchicine responsible for high affinity binding to **tubulin** and is reviewed for analogs in the colchicine series. The thermodynamic and kinetic aspects of the association are described and evaluated in terms of the binding mechanism. Colchicine binding to **tubulin** results in unusual alterations in the low energy electronic spectra of colchicine. The spectroscopic features of colchicine bound to **tubulin** are discussed in terms of the nature of the colchicine-**tubulin** complex. Attempts to locate the high affinity colchicine binding site on **tubulin** are presented.

L46 ANSWER 23 OF 33 JICST-EPlus COPYRIGHT 2006 JST on STN

ACCESSION NUMBER: 900643578 JICST-EPlus
TITLE: Rapid induction of synthesis and doubling of nuclear DNA by benzyladenine in intact bean leaves.
AUTHOR: MOMOTANI E; TSUJI H
KINOSHITA I; YOKOMURA E
CORPORATE SOURCE: Kyoto Univ., Kyoto, JPN
Nara Women's Univ., Nara, JPN
SOURCE: Plant Cell Physiol, (1990) vol. 31, no. 5, pp. 621-625.
Journal Code: F0964A (Fig. 3, Tbl. 1, Ref. 11)
CODEN: PCPHA5; ISSN: 0032-0781
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article

LANGUAGE: English
STATUS: New
AB Primary leaves of young and old bean plants (Phaseolus vulgaris L.) were treated with benzyladenine(BA) after cell division had been completed. Changes in the synthesis and amount of DNA in individual nuclei in mesophyll cells shortly after BA application were studied. Cytofluorometric determination of nuclear DNA with 4',6-diamidino-2-phenylindole(**DAPI**) showed that cells containing 4C nuclei had appeared in both young and old leaves by 24h after BA application, while the nuclear DNA content in control leaves remained at 2C. The number of 4C nuclei increased until 48h in young leaves, but not in old leaves. Autoradiographic analysis showed that nuclei labelled with ¢6-3H!thymidine increased over the control level 12h after BA application. This effect peaked at 24h followed by a decline. There was no difference in the initial effect between young and old leaves, but the effect diminished more rapidly in old leaves than in young ones. The results are discussed in relation to those obtained from DNA measurements long after BA application in previous studies. (author abst.)

L46 ANSWER 24 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1988:270638 BIOSIS
DOCUMENT NUMBER: PREV198886009882; BA86:9882
TITLE: MICROTUBULES IN ASCIDIAN EGGS DURING MEIOSIS FERTILIZATION AND MITOSIS.
AUTHOR(S): SAWADA T-O [Reprint author]; SCHATTEN G
CORPORATE SOURCE: INTEGRATED MICROSCOPY RESORCE BIOMED RES, ZOOL RES BUILD, UNIV WISCONSIN, 1117 W JOHNSON ST, MADISON, WIS 53706, USA
SOURCE: Cell Motility and the Cytoskeleton, (1988) Vol. 9, No. 3, pp. 219-230.
CODEN: CMCYEO. ISSN: 0886-1544.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 2 Jun 1988
Last Updated on STN: 2 Jun 1988
AB The sequential changes in the distribution of microtubules during germinal vesicle breakdown (GVBD), fertilization, and mitosis were investigated with **antitubulin** indirect **immunofluoresence** microscopy in **several** species of ascidian eggs (Molgula occidentalis, Ciona savignyi, and Halocynthia roretzi). These alterations in microtubule patterns were also correlated with observed cytoplasmic movements. A cytoplasmic latticework of microtubules was observed throughout meiosis. The unfertilized egg of M. occidentalis had a small meiotic spindle with wide poles; the poles became focused after egg activation. The other two species had more typical meiotic spindles before fertilization. At fertilization, a sperm aster first appeared near the cortex close to the vegetal pole. It enlarged into an unusual asymmetric aster associated with the egg cortex. The sperm aster rapidly grew after the formation of the second polar body, and it was displaced as far as the equatorial region, corresponding to the site of the myoplasmic crescent, the posterior half of the egg. The female pronucleus migrated to the male pronucleus at the center of the sperm aster. The microtubule latticework and the sperm aster disappeared towards the end of first interphase with only a small bipolar structure remaining until first mitosis. At mitosis the asters enlarged tremendously, while the mitotic spindle remained remarkably small. The two daughter nuclei remained near the site of cleavage even after division was complete. These results document the changes in microtubule patterns during maturation in Ascidian oocytes, demonstrate that the sperm contributes the active centrosome at

fertilization, and reveal the presence of a mitotic apparatus at first division which has an unusually small spindle and huge asters.

L46 ANSWER 25 OF 33 MEDLINE on STN
ACCESSION NUMBER: 85131048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3972806
TITLE: 4',6-Diamidino-2-phenylindole, a fluorescent probe for **tubulin** and microtubules.
AUTHOR: Bonne D; Heusele C; Simon C; Pantaloni D
SOURCE: The Journal of biological chemistry, (1985 Mar 10) Vol. 260, No. 5, pp. 2819-25.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198504
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 11 Apr 1985
AB A new fluorophor for **tubulin** which has permitted the monitoring of microtubule assembly in vitro is reported. **DAPI** (4',6-diamidino-2-phenylindole), a fluorophor already known as a DNA intercalator, was shown to bind specifically to a unique **tubulin** site as a **dimer** (KD(app) = 43 +/- 5 microM at 37 degrees C) or to **tubulin** associated in microtubules (KD(app) = 6 +/- 2 microM at 37 degrees C) with the same maximum enhancement in fluorescence. When **tubulin** polymerization was induced with GTP, the change in **DAPI** affinity for **tubulin** resulted in an enhancement of **DAPI** binding and, consequently, of fluorescence intensity. **DAPI**, whose binding site is different from that of colchicine, vinblastine, or taxol, did not interfere greatly with microtubule polymerization. It induced a slight diminution of the critical concentration for **tubulin** assembly due to a decrease in the depolymerizing rate constant. Moreover, **DAPI** did not interfere with GTP hydrolysis correlated with **tubulin** polymerization, but it decreased the GTPase activity at the steady state of **tubulin** assembly. Even at substoichiometric levels **DAPI** can be used to follow the kinetics of microtubule assembly.

L46 ANSWER 26 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 86099083 EMBASE
DOCUMENT NUMBER: 1986099083
TITLE: A fluorometric assay for the **biotin-avidin** interaction based on displacement of the fluorescent probe 2-anilinonaphthalene-6-sulfonic acid.
AUTHOR: Mock D.M.; Langford G.; Dubois D.; et al.
CORPORATE SOURCE: Department of Biochemistry, University of Texas Health Science Center, San Antonio, TX 78284, United States
SOURCE: Analytical Biochemistry, (1985) Vol. 151, No. 1, pp. 178-181. .
CODEN: ANBCA2
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991
AB **Avidin** and **biotin** can be sensitively and accurately

quantitated using the fluorescent probe 2-anilinonaphthalene-6-sulfonic acid (2,6-**ANS**). In the presence of **avidin**, the fluorescence of 2,6-**ANS** is blue shifted with a large increase in quantum yield. **Biotin** binding causes complete displacement of the bound fluorophore with concomitant quenching of the fluorescence. The fluorometric monitoring of the displacement of 2,6-**ANS** can be used as a facile method of measuring the **biotin-avidin** interaction. 2,6-**ANS** displacement gives the same stoichiometry as the method using 4'-hydroxyazobenzene-2-carboxylic acid. Our initial studies of an affinity-purified **avidin** revealed that, of the four binding sites on the **avidin** tetramer, a mean of three remain available for **biotin** (or dye) binding; this finding highlights a caveat concerning the use of affinity-purified **oligomeric**-binding proteins with multiple sites. As compared with previous fluorescence methods, the use of 2,6-**ANS** gives high sensitivity without the necessity of preparing and purifying a covalent **avidin** conjugate. In addition, the present method: is potentially more sensitive than those based on optical absorbance; uses a probe that has increased stability and a larger Stokes shift compared with fluorescein; is not subject to protein interference; and gives accurate results over a wide range of 2,6-**ANS** and **avidin** concentrations.

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ACCESSION NUMBER: 79124428 EMBASE
DOCUMENT NUMBER: 1979124428
TITLE: Aggregation of microtubule initiation sites preceding neurite outgrowth in mouse neuroblastoma cells.
AUTHOR: Spiegelman B.M.; Lopata M.A.; Kirschner M.W.
CORPORATE SOURCE: Dept. Biochem. Sci., Princeton Univ., Princeton, N.J. 08540, United States
SOURCE: Cell, (1979) Vol. 16, No. 2, pp. 253-263. .
CODEN: CELLB5
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English

AB By examining microtubule regrowth using immunofluorescence with antibody to **tubulin**, we have studied the structure and intracellular localization of microtubule initiation sites in undifferentiated and differentiated mouse neuroblastoma cells. The undifferentiated cells are round and lack cell processes. They contain an average of 12 initiation sites per cell. Each of these sites, which are located near the cell nucleus, initiates the growth of **several microtubules** in a radial formation. In contrast to the undifferentiated cells, neuroblastoma cells stimulated to differentiate by serum deprivation are asymmetrical, containing one or two very long neurites. These cells have a single, large microtubule initiation center which can be visualized not only by **immunofluoresence** but by phase-contrast and differential interference microscopy as well. The initiation site measures 3-4 μ in diameter and is located in the cell body along a line defined by the neurite. During cell differentiation, the large initiation center seems to be formed by the aggregation of many smaller sites. This process precedes neurite extension by about 24 hr. The growth of microtubules from this center appears to be highly oriented, since most microtubules initially grow into the neurite processes rather than into the cell interior. Thus major changes in the structure and location of microtubule

initiation sites occur during the differentiation of neuroblastoma cells. Similar changes are likely to be involved in alterations in the morphology of other cell types.

L46 ANSWER 28 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 79037373 EMBASE
DOCUMENT NUMBER: 1979037373
TITLE: Kinetics and mechanism of colchicine binding to **tubulin**: Evidence for ligand-induced conformational change.
AUTHOR: Garland D.L.
CORPORATE SOURCE: Lab. Biochem., Sect. Enz., Nat. Heart Lung Blood Inst., NIH, Bethesda, Md. 20014, United States
SOURCE: Biochemistry, (1978) Vol. 17, No. 20, pp. 4266-4272. . CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
030 Pharmacology
LANGUAGE: English

AB The kinetics of **tubulin**-colchicine complex formation were reinvestigated using both isotopic labeling and fluorescence techniques. The time course for association is composed of a relatively fast step, which is responsible for most of the reaction, followed by a slower step, which accounted for 5-10% of the bound colchicine. The origin of the slow step is not known. Analysis of the fast step showed that, under pseudo-first-order conditions, rate constants for association, k(obsd), increased linearly with both increasing colchicine and **tubulin** concentration and then deviated from linearity at high concentrations. Plots of (k(obsd) - k -2)-1 vs. concentration-1 were linear. The simplest mechanism that can explain the data is: P + C (k1→) (K-1←)PC (K2→)(K-2←)(PC)', (arrows indicating forward and reverse rate constants.) Kinetic constants were obtained by computer curve fitting of the data. These yield an equilibrium constant for the rapid equilibrium step K1 = 6 x 103 M-1; k2 = (2-3) x 103 sec-1 and k-2 = (5-9) x 10-6 sec-1. The rate constant for the dissociation of the **tubulin** -colchicine complex determined by the isotopic labeling method was 5.3 x 10-6 sec-1. Therefore, k-2 is the rate-limiting step for colchicine dissociation from the **tubulin**-colchicine complex. The dependency of k(obsd) on solvent viscosity was determined using sucrose to vary the viscosity. At low colchicine concentrations the apparent second-order rate constant is decreased with increasing viscosity, whereas at high colchicine concentrations the rate dependency on viscosity is significantly reduced. The fluorescence enhancement observed when colchicine binds to **tubulin** is a consequence of the colchicine-induced conformational change step. **Tubulin** prepared by cycles of polymerization-depolymerization was separated into two molecular weight species [Weingarten, M. D., Suter, M.M., Littman, D.R., and Kirschner, M.W. (1974), Biochemistry 13, 5529], peak 1 containing the high-molecular-weight species and peak 2 consisting only of **tubulin dimers.** The apparent second-order rate constants for association of colchicine to **tubulin** in both peaks were essentially the same, 1.7 and 1.4 x 102M-1sec -1, respectively. When **tubulin** was preincubated with colchicine prior to chromatography, bound colchicine was only found in peak 2 as the **tubulin dimer.**

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reserved on STN
ACCESSION NUMBER: 78326161 EMBASE
DOCUMENT NUMBER: 1978326161
TITLE: An effect of fluorescent probes and of insulin on the structure of adipocyte membranes.
AUTHOR: Bailey I.A.; Garratt C.J.; Wallace S.M.
CORPORATE SOURCE: Dept. Chem., Univ. York, Heslington Y01 5DD, United Kingdom
SOURCE: Biochemical Society Transactions, (1978) Vol. 6, No. 1, pp. 302-304. .
CODEN: BCSTB5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
LANGUAGE: English
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L46 ANSWER 30 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1978:141276 BIOSIS
DOCUMENT NUMBER: PREV197865028276; BA65:28276
TITLE: PHYSICAL CHEMICAL STUDY OF DAUNOMYCIN **TUBULIN** INTERACTIONS.
AUTHOR(S): NA C [Reprint author]; TIMASHEFF S N
CORPORATE SOURCE: GRAD DEP BIOCHEM, BRANDEIS UNIV, WALTHAM, MASS 02154, USA
SOURCE: Archives of Biochemistry and Biophysics, (1977) Vol. 182, No. 1, pp. 147-154.
CODEN: ABBIA4. ISSN: 0003-9861.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The interaction of the antitumor agent daunomycin with calf brain **tubulin** was examined by spectroscopic and sedimentation techniques. Spectrofluorometric studies resulted in a Ka of 3.6 + 103 M-1 at 20° C and a binding stoichiometry of 2 daunomycin molecules/**tubulin** 110,000 MW **dimer.** The association reaction has a negative enthalpy change which, in accord with the results of the differential spectroscopic studies, suggests that daunomycin binds to **tubulin** through H bonding and/or electrostatic interactions. Sedimentation velocity studies, using an analytical ultracentrifuge equipped with an optical scanner, showed that daunomycin binds to the 5.8 S **tubulin dimer** and the 42 S double-ring structures. At concentrations above 2.5 + 10-5 M, daunomycin perturbs the Mg2+-induced **tubulin** polymerization toward dissocation of the polymers and inhibits in vitro microtubule assembly.

L46 ANSWER 31 OF 33 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 78096041 EMBASE
DOCUMENT NUMBER: 1978096041
TITLE: 1 anilino 8 naphthalenesulfonate: a fluorescent probe of ion and ionophore transport kinetics and trans membrane asymmetry.
AUTHOR: Haynes D.H.; Simkowitz P.
CORPORATE SOURCE: Dept. Pharmacol., Univ. Miami Med. Sch., Miami, Fla. 33152, United States
SOURCE: Journal of Membrane Biology, (1977) Vol. 33, No. 1-2, pp. 63-108. .
CODEN: JMBBBO
COUNTRY: Germany

DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
002 Physiology
LANGUAGE: English

AB The kinetics of the transport of the 1 anilino 8 naphthalenesulfonate (**ANS**-, an anionic fluorescent probe of the membrane surface) across phospholipid vesicle membranes have been studied using a stopped flow rapid kinetic technique. The method has been used to gain detailed information about the mechanism of transport of this probe and to study ionophore mediated cation transport across the membrane. The technique has also been exploited to study differences between the inside and outside surfaces of vesicles containing phosphatidyl choline (PC). Binding of **ANS**- on the outside surface occurs within times shorter than 100 μsec while permeation occurs in the time range 5 to 100 sec. Net transport of **ANS**- occurs with cotransport of alkali cations. The transport rate is maximal in the region of the crystalline to liquid crystalline phase transition, and the increase correlates with changes in the degree of aggregation of the vesicles. Incorporation of phosphatidic acid (PA), phosphatidyl ethanolamine (PE) or cholesterol into PC membranes decreases the rate of **ANS**- transport. Neutral ionophores (I) of the valinomycin type increase **ANS**- permeability in the presence of alkali cations (M+) by a mechanism involving the transport of a ternary I-M+ **ANS**- complex. The equilibrium constants for formation of these complexes and their rate constants for their permeation are presented. The maximal turnover number for **ANS**- transport by valinomycin in dimyristoyl PC vesicles at 35°C was 46 per sec. The partitioning of the ionophore between the aqueous and membrane phases and the rate of transfer of an ionophore from one membrane have been determined in kinetic experiments. A method is described for the detection of I-M+ complexes on the membrane surface by their enhancement effects on **ANS**- fluorescence at temperature below the phase transition temperature on 'monolayer' vesicles. The apparent stability constants for several I-M+ complexes are given. Analysis of the effect of ionic strength on the **ANS**- binding to the inside outside surfaces indicates that the electrostatic surface potential (at fixed ionic strength and surface change) is larger for the inside surface than for the outside surface. Analysis of the dependence of the maximal **ANS**- binding for the inside and outside surfaces of vesicles made from PC and a variable mole fraction of PA, PE or cholesterol indicates that the latter 3 are located preferentially on the inside surface.

L46 ANSWER 32 OF 33 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 76069257 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1194282
TITLE: Interaction of Vinblastine with Calf Brain Microtubule protein.
AUTHOR: Lee J C; Harrison D; Timasheff S N
SOURCE: The Journal of biological chemistry, (1975 Dec 25) Vol. 250, No. 24, pp. 9276-82.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197602
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 9 Feb 1976

AB The interaction of vinblastine with calf brain **tubulin** has been studied by velocity sedimentation, gel filtration, and fluorescence. It has been established that vinblastine induces the stable **tubulin dimers** to **dimerize** further to tetramers. The sedimentation patterns at low vinblastine concentration were analyzed by the ligand-induced **dimerization** theory of Cann and Goad ((1972) Arch. Biochem. Biophys. 153, 603-609). The association constant and stoichiometry for the binding of vinblastine to **tubulin**, determined by gel filtration and **spectrofluorometry**, were (2.3 +/- 0.1) X 10(4) liters/mol at 25 degrees and two vinblastine binding sites per **tubulin dimer** of molecular weight 110,000. The binding of vinblastine to **tubulin** is characterized by an enthalpy change of 5.8 kcal/mol and a positive unitary entropy change. Binding of vinblastine did not induce any significant conformational changes in **tubulin** as monitored by circular dichroism. However, the vinblastine-**tubulin** complex displayed an ultraviolet difference spectrum, which appears to reflect mostly the transfer of vinblastine to a less polar environment. Besides binding vinblastine, **tubulin** was shown to bind vincristine with identical free energy and stoichiometry and to have a single binding site for 8-anilino-1-naphthalene sulfonic acid per **tubulin dimer** , which is independent of those for vinblastine.

L46 ANSWER 33 OF 33 MEDLINE on STN
ACCESSION NUMBER: 76039904 MEDLINE
DOCUMENT NUMBER: PubMed ID: 241381
TITLE: Structural role of pyridoxal 5'-phosphate, pyridoxal 5'-phosphate analogs, and other agents in the association of subunits of Bacillus alvei apotryptophanase.
AUTHOR: Isom H C; DeMoss R D
SOURCE: Biochemistry, (1975 Sep 23) Vol. 14, No. 19, pp. 4298-304. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197601
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 23 Jan 1976

AB Bacillus alvei apotryptophanase readily dissociates at low protein concentration and sediments at 5.7 S (**dimer**) in 0.01 M potassium phosphate (pH 7.8) from 9 to 33 degrees. With temperature held constant at 9 degrees, increasing the potassium, sodium, or ammonium phosphate buffer concentration increases the sedimentation value to 8.0 S. Increasing the monovalent cation concentration alone does not have the effect. Imidazole and pyridoxal compete with phosphate, preventing the effect. Raising the temperature to 26 degrees in the presence of high concentrations of potassium phosphate increases the sedimentation constant to 9.4 S. The addition of pyridoxal-P converts the **dimer** to a 9.4S tetramer. The conversion is dependent upon coenzyme concentration, temperature, and the nature of monovalent cation present. The Km for pyridoxal-P for the sodium form of the enzyme is more than tenfold greater than the Km for the potassium form of the enzyme. 2'-Methyl, 2'-hydroxyl, 6-methyl, and the N-oxide of pyridoxal-P are active in the association of **dimer** to tetramer but to differing extents. Analogs altered in the 4'-formyl position are also inactive structurally. Anthranilic acid, a competitive inhibitor of tryptophan, and 8-anilino-1-naphthalenesulfonic acid (**ANS**), a competitive inhibitor of pyridoxal-P binding, are both active in affecting the **dimer** to tetramer association but

tryptophan is not. The **dimer** and tetramer are spectrally distinguishable through circular dichroic measurements, fluroescence quenching with pyridoxal-P or pyridoxal, and fluorescence enhancement with **ANS**. Pyridoxal-P causes the release of **ANS** from an **ANS**-apoenzyme complex.

```
=> d que stat l49
L5          1239 SEA FILE=REGISTRY ABB=ON  TUBULIN?/CN
L6             1 SEA FILE=REGISTRY ABB=ON  DAPI/CN
L7             2 SEA FILE=REGISTRY ABB=ON  ANS/CN
L8             1 SEA FILE=REGISTRY ABB=ON  82-76-8
L9             2 SEA FILE=REGISTRY ABB=ON  BIS-ANS/CN
L10            1 SEA FILE=REGISTRY ABB=ON  "NPN 3"/CN
L11            1 SEA FILE=REGISTRY ABB=ON  "NAPHTHYLENE DIISOCYANATE"/CN
L12            2 SEA FILE=REGISTRY ABB=ON  "RUTHENIUM RED"/CN
L13            1 SEA FILE=REGISTRY ABB=ON  DCVJ/CN
L14            1 SEA FILE=REGISTRY ABB=ON  "CRESOL FAST VIOLET"/CN
L15           11 SEA FILE=REGISTRY ABB=ON  L6 OR L7 OR L8 OR L9 OR L10 OR L11
                  OR L12 OR L13 OR L14
L16         1250 SEA FILE=REGISTRY ABB=ON  L15 OR L5
L29        31490 SEA FILE=HCAPLUS ABB=ON  L16 OR ?TUBULIN? OR ?DAPI? OR
                  ?ANILINONAPHTHALENE?(W)?SULFONATE? OR ANS OR BIS(W)ANS OR
                  BIS(W)?ANILINONAPHTHALENE?(W)?SULFONATE? OR N(W)PHENYL(W)1(W)?N
                  APHTHYLENE? OR NPN OR ?RUTHENIUM?(W)RED? OR ?CRESOL?(W)?VIOLET?
                   OR DCVJ OR ?JULOLIDINE?
L30          479 SEA FILE=HCAPLUS ABB=ON  L29 AND (?FLUOROMETRY? OR ?FLUORESENC?
                  )
L31           18 SEA FILE=HCAPLUS ABB=ON  L30 AND  DRUG(W)(SCREEN OR SCREENING)
L32           25 SEA FILE=HCAPLUS ABB=ON  L30 AND (?MONOMER? OR ?DIMER? OR
                  ?OLIGOMER? OR ?MICROTUBUL?(5A)?SEVER? OR ?TUBUL?(4A)?SEVER?)
L33           40 SEA FILE=HCAPLUS ABB=ON  L31 OR L32
L34            8 SEA FILE=HCAPLUS ABB=ON  L33 AND ?TEST?
L35           40 SEA FILE=HCAPLUS ABB=ON  L34 OR L33
L36            2 SEA FILE=REGISTRY ABB=ON  (AVIDIN OR BIOTIN)/CN
L37            4 SEA FILE=HCAPLUS ABB=ON  L35 AND (?MICROTUBUL?(W)?MOTOR?(W)?PRO
                  TEIN? OR L36 OR ?AVIDIN? OR ?BIOTIN? OR ?ANTI?(W)?TUBULIN(W)?AN
                  TIBOD? OR ?MICROTUBUL?(W)?BIND?(W)?PROTEIN? OR MAP)
L39            1 SEA FILE=HCAPLUS ABB=ON  L35 AND (?POLYARGININE? OR ?POLYHISTID
                  INE? OR ?POLYLYSINE?)
L40            1 SEA FILE=HCAPLUS ABB=ON  L35 AND ?CONTACT?(4A)(?TUBULIN? OR
                  ?MICROTUBULE?)
L41           40 SEA FILE=HCAPLUS ABB=ON  L35 OR L37 OR L39 OR L40
L42           35 SEA FILE=HCAPLUS ABB=ON  L41 AND (PRD<20040120 OR PD<20040120)
L43            1 SEA FILE=HCAPLUS ABB=ON  L42 AND ?DEPOLYMERIZ?(4A)?INHIBIT?
L48          280 SEA FILE=USPATFULL ABB=ON  L42 OR L43
L49            2 SEA FILE=USPATFULL ABB=ON  L48 AND ?DEPOLYMERIZ?(4A)?INHIBIT?

=> d ibib abs hitstr l49 1-2

L49  ANSWER 1 OF 2  USPATFULL on STN
ACCESSION NUMBER:        2002:273452  USPATFULL
TITLE:                   Synthetic spiroketal pyranes as potent anti-cancer
                         agents and use
INVENTOR(S):             Uckun, Fatih M., White Bear Lake, MN, UNITED STATES
                         Mao, Chen, St. Paul, MN, UNITED STATES
                         Huang, He, New Brighton, MN, UNITED STATES
PATENT ASSIGNEE(S):      Parker Hughes Institute, Roseville, MN, UNITED STATES
                         (U.S. corporation)

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2002151580      A1   20021017            <--
                         US 6512003         B2   20030128
APPLICATION INFO.:       US 2001-974070     A1   20011009  (9)
RELATED APPLN. INFO.:    Continuation of Ser. No. US 1999-352648, filed on 29
                         Jun 1999, GRANTED, Pat. No. US 6335364
```

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-91002P	19980629 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel **tubulin** binding compounds (SPIKETS) having potent **tubulin depolymerization** activity and **inhibitory** activity against **tubulin** polymerization. The compounds are effective agents for inhibiting cellular proliferation, for example, in cancer cells. The compounds are adapted to interact favorably with a novel SP binding pocket on **tubulin** , which pocket is useful for screening of anti-**tubulin**, anti-proliferation, and anti-cancer drugs.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L49 ANSWER 2 OF 2 USPATFULL on STN
ACCESSION NUMBER: 2002:1257 USPATFULL
TITLE: Synthetic spiroketal pyranes as potent anti-cancer agents
INVENTOR(S): Uckun, Faith M., White Bear Lake, MN, United States
Mao, Chen, St. Paul, MN, United States
Huang, He, New Brighton, MN, United States
PATENT ASSIGNEE(S): Parker Hughes Institute, Roseville, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 6335364	B1	20020101		<--
APPLICATION INFO.:	US 1999-352648		19990629	(9)	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-91002P	19980629 (60)	<--
	US 1998-91002P	19980629 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lambkin, Deborah C.
LEGAL REPRESENTATIVE: Merchant & Gould P.C.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel **tubulin** binding compounds (SPIKETS) having potent **tubulin depolymerization** activity and **inhibitory** activity against **tubulin** polymerization. The compounds are effective agents for inhibiting cellular proliferation, for example, in cancer cells. The compounds are adapted to interact favorably with a novel SP binding pocket on **tubulin** , which pocket is useful for screening of anti-**tubulin**, anti-proliferation, and anti-cancer drugs.

=> d ibib abs ind l3 1-3

L3 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:711995 HCAPLUS
DOCUMENT NUMBER: 132:1304
TITLE: Microtubule disassembly by ATP-dependent oligomerization of the AAA enzyme katanin
AUTHOR(S): **Hartman, James J.; Vale, Ronald D.**
CORPORATE SOURCE: The Howard Hughes Medical Institute and the Department of Cellular and Molecular Pharmacology, University of California, San Francisco, CA, 94143, USA
SOURCE: Science (Washington, D. C.) (1999), 286(5440), 782-785
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Katanin (I), a microtubule-stimulated ATPase of the AAA (ATPase-associated activities) enzyme superfamily, uses nucleotide hydrolysis energy to sever and disassemble microtubules. Many AAA enzymes disassemble stable protein-protein complexes, but their mechanisms are not well understood. Here, a fluorescence resonance energy transfer assay demonstrated that the p60 subunit of I oligomerized in an ATP- and microtubule-dependent manner. Oligomerization increased the affinity of I for microtubules and stimulated its ATPase activity. After hydrolysis of ATP, microtubule-bound I oligomers disassembled microtubules and then dissociated into free I monomers. Coupling a nucleotide-dependent oligomerization cycle to the disassembly of a target protein complex may be a general feature of ATP-hydrolyzing AAA domains.
CC 6-1 (General Biochemistry)
Section cross-reference(s): 7
ST microtubule disassembly katanin ATPase ATP dependent oligomerization
IT Microtubule
(microtubule disassembly by ATP-dependent oligomerization of the ATPase katanin)
IT Polymerization
(oligomerization; microtubule disassembly by ATP-dependent oligomerization of the ATPase katanin)
IT Quaternary structure
(protein; microtubule disassembly by ATP-dependent oligomerization of the ATPase katanin)
IT 9000-83-3, ATPase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(katanin; microtubule disassembly by ATP-dependent oligomerization of the ATPase katanin)
IT 56-65-5, 5'-ATP, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(microtubule disassembly by ATP-dependent oligomerization of the ATPase katanin)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:673147 HCAPLUS
DOCUMENT NUMBER: 131:308619
TITLE: Assays for the detection of microtubule depolymerization inhibitors
INVENTOR(S): **Vale, Ronald D.; Hartman, James J.**

PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953295	A1	19991021	WO 1999-US8086	19990413
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937457	A1	19991101	AU 1999-37457	19990413
EP 1071943	A1	20010131	EP 1999-919826	19990413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6410687	B1	20020625	US 1999-291170	19990413
JP 2002522747	T2	20020723	JP 2000-543811	19990413
US 6429304	B1	20020806	US 2000-724884	20001128
US 6699969	B1	20040302	US 2000-724592	20001128
US 6872537	B1	20050329	US 2000-673222	20001204
US 2004161784	A1	20040819	US 2004-761781	20040120
US 2005164230	A1	20050728	US 2004-927588	20040825

PRIORITY APPLN. INFO.:

US 1998-81734P	P	19980414
US 1999-291170	A3	19990413
WO 1999-US8086	W	19990413
US 2000-673322	A1	20001013
US 2000-673222	A1	20001204

AB This invention provides methods for the screening and identification of agents having potent effects on the progression of the cell cycle. In one embodiment, the methods involve contacting a polymerized microtubule with a microtubule severing protein or a microtubule depolymg. protein in the presence of an ATP or a GTP and a test agent; and (ii) detecting the formation of tubulin monomers, dimers or oligomers. The p60 subunit of katanin provides a particularly preferred microtubule severing protein possessing both ATPase and microtubule severing activities.

IC ICM G01N021-03
ICS G01N021-07; G01N021-17; G01N021-25; G01N021-31; G01N021-33; G01N033-48; G01N033-483; G01N033-50; G01N033-52

CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 3, 7, 63

ST microtubule depolymn inhibitor

IT Mitosis
(Antimitotic agents; assays for detection of microtubule depolymn. inhibitors)

IT Animal tissue culture
Apparatus
Baculoviridae
Cell cycle
Centrifugation
Containers
Cytoskeleton

Databases
Depolymerization
Drug screening
Drugs
Immunoassay
Microtiter plates
Microtubule
Molecular cloning
Polymerization
Test kits
(assays for detection of microtubule depolymn. inhibitors)

IT Nucleic acids
Promoter (genetic element)
Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(assays for detection of microtubule depolymn. inhibitors)

IT Avidins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(assays for detection of microtubule depolymn. inhibitors)

IT Fluorometry
(fluorescent resonance energy transfer; assays for detection of microtubule depolymn. inhibitors)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene KCM1, from Xenopus; assays for detection of microtubule depolymn. inhibitors)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(katanin; assays for detection of microtubule depolymn. inhibitors)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(microtubule depolymg.; assays for detection of microtubule depolymn. inhibitors)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(microtubule motor; assays for detection of microtubule depolymn. inhibitors)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(microtubule severing; assays for detection of microtubule depolymn. inhibitors)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(microtubule-binding; assays for detection of microtubule depolymn. inhibitors)

IT Phosphoproteins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(stathmins, OP18; assays for detection of microtubule depolymn. inhibitors)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(to tubulin; assays for detection of microtubule depolymn. inhibitors)
IT Oligomers
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tubulin; assays for detection of microtubule depolymn. inhibitors)
IT 58293-56-4, DCVJ
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DCJV; assays for detection of microtubule depolymn. inhibitors)
IT 82-76-8, Ans 569-64-2, Malachite green 65664-81-5, Bis-ANS
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(assays for detection of microtubule depolymn. inhibitors)
IT 11103-72-3, Ruthenium red 18472-89-4, Cresyl violet 47165-04-8, Dapi
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(assays for detection of microtubule depolymn. inhibitors)
IT 9000-83-3, ATPase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(assays for detection of microtubule depolymn. inhibitors)
IT 56-65-5, Atp, biological studies 58-85-5, Biotin 86-01-1, Gtp 173247-44-4 213614-51-8 213614-52-9
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(assays for detection of microtubule depolymn. inhibitors)
IT 86-01-1D, Gtp, analogs 24937-47-1, Polyarginine 25104-18-1, Polylysine 25212-18-4, Polyarginine 26062-48-6, Polyhistidine 26854-81-9, Polyhistidine 33069-62-4, Paclitaxel 33069-62-4D, Paclitaxel, analogs 38000-06-5, Polylysine
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(assays for detection of microtubule depolymn. inhibitors)
IT 134711-01-6, Protein (Saccharomyces cerevisiae clone pRC111 gene PAS1 reduced) 147279-29-6, Protein (Escherichia coli strain W3110 gene ftsH reduced) 147784-94-9, RNA formation factor (Saccharomyces cerevisiae gene SUG1 reduced) 158454-79-6 189086-69-9 213614-53-0, Katanin (human hippocampus p80 subunit) 247584-42-5
RL: PRP (Properties)
(unclaimed protein sequence; assays for the detection of microtubule depolymn. inhibitors)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:288406 HCAPLUS
DOCUMENT NUMBER: 129:256705
TITLE: Katanin, a microtubule-severing protein, is a novel AAA ATPase that targets to the centrosome using a WD40-containing subunit
AUTHOR(S): **Hartman, James J.**; Mahr, Jeff; McNally, Karen; Okawa, Katsuya; Iwamatsu, Akihiro; Thomas, Susan; Cheesman, Sarah; Heuser, John; **Vale, Ronald D.**; McNally, Francis J.
CORPORATE SOURCE: Howard Hughes Medical Inst., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Cell (Cambridge, Massachusetts) (1998), 93(2), 277-287
CODEN: CELLB5; ISSN: 0092-8674
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Microtubule disassembly at centrosomes is involved in mitotic spindle

function. The microtubule-severing protein katanin, a heterodimer of 60 and 80 kDa subunits, was previously purified and shown to localize to centrosomes in vivo. Here the authors report the sequences and activities of the katanin subunits. The p60 subunit is a new member of the AAA family of ATPases, and expressed p60 has microtubule-stimulated ATPase and microtubule-severing activities in the absence of p80. The p80 subunit is a novel protein containing WD40 repeats, which are frequently involved in protein-protein interactions. The p80 WD40 domain does not participate in p60 dimerization, but localizes to centrosomes in transfected mammalian cells. These results indicate katanin's activities are segregated into a subunit (p60) that possesses enzymic activity and a subunit (p80) that targets the enzyme to the centrosome.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 7, 12, 13

ST katanin ATPase subunit centrosome targeting; cDNA sequence katanin ATPase human Strongylocentrotus

IT Protein motifs
(WD40 domain; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT Organelle
(centrosome; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT Biological transport
(intracellular; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT Microtubule
Protein sequences
Strongylocentrotus purpuratus
cDNA sequences
(katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(katanin; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT 9000-83-3, ATPase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(AAA; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT 213614-51-8 213614-52-9 213614-53-0, Katanin (human hippocampus p80 subunit)
RL: PRP (Properties)
(amino acid sequence; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

IT 206230-94-6, GenBank AF052432 206230-95-7, GenBank AF052433 207530-04-9, GenBank AF052191
RL: PRP (Properties)
(nucleotide sequence; katanin is an AAA ATPase that targets to centrosome using WD40 repeat-containing p80 subunit)

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT